Sickle Cell Anaemia in Kuwait

Parents knowledge about the genetic transmission, their reproductive practices and their attitudes towards screening

by

Sana' Adel Saqf El-Hait

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Centre for International Child Health
Institute of Child Health
University of London
30 Guilford Street
London WC1N 1EH

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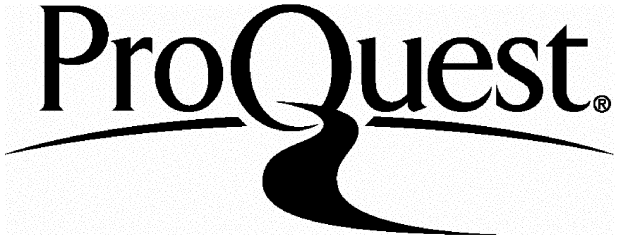


D e d i c a t i o n

To my ever loving, ever giving ever caring

F a t h e r

To my Father whose

- **main concern has always been my happiness and my success.**
- **main worry during the Gulf War was my safety and my MSc dissertation.**
- **who has always been the best example for me to keep going regardless of any obstacle**

May Allah give him a healthy long life

and

to the soul of my Mother, may she rest in peace. May mercy from Allah be upon her.

Abstract

• **Objectives**
To determine the quality of knowledge about the genetic transmission of sickle cell disease (SCD) among parents of affected children, to describe their reproductive behaviour and to ascertain their attitudes towards screening.

• **Design**
Cross sectional study in July - August 1990.

• **Setting**
The haematology unit of the paediatric department of Sabah Hospital in Kuwait.

• **Subjects**
52 families, responded as couples (51.4%), mothers (37.2%) and fathers (11.4%), aged 24 - 55 years. Consanguinity (first cousin) among them was 61.6% (30.8%)

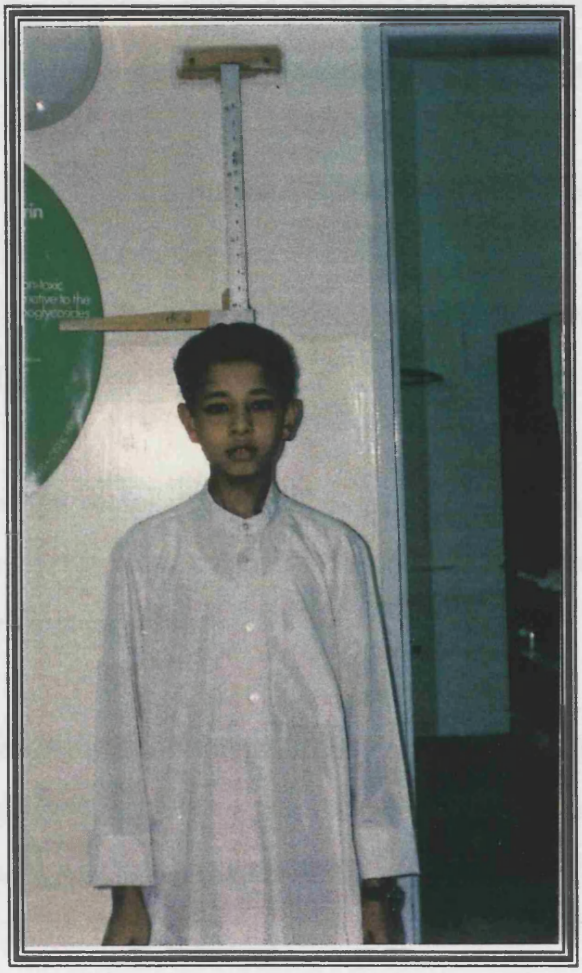
• **Results:**

- Knowledge about the disease genetic transmission
50% of parents scored "good" knowledge, 27% scored fair, and 23% low knowledge. 90% knew it is inherited, 59% knew it is transmitted from both parents, 70% were aware of the presence of a carrier in their children, only 42% knew that the risk persists in each pregnancy, 92% thought there is an increased risk of cousins' marriages. Mass media was a source of information in only 27% , and 23% knew about a relative affected before they have had planned for the affected child.

- Reproductive behaviour
Mean number of pregnancies before diagnosis of the first affected child was 3.7 (SD 2.5), and after diagnosis 2 (SD 1.8). Parents' decision was influenced by the family size rather than by their socio-economic conditions or by their knowledge about the disease. Mean number of children among those who intend to have more children in spite of SCD diagnosis was 3.7 (SD 1.6), and among those who did not intend to have more 5.6 (SD 2). Only 9.6% stopped further pregnancies because of diagnosis of an affected child. The 40% who used contraceptive measures wanted to space pregnancies and not to limit the family size.

- Attitudes
The best age for information transfer (by 72%) about the genetic transmission was 15 years. All the 70% who were aware of the presence of a carrier among their children would advise their children to disclose about it to their partners in the future. 96% wanted to screen before marriage. Divorce rate because of the disease 5.7% compared to 1.7% among Kuwaiti population. Almost all 96% voted for neonatal screening. 73% would choose prenatal diagnosis if it were available in Kuwait, but only 31% would terminate an affected foetus.

• **Conclusion**
Although some parents of SCD patients in Kuwait were rather knowledgeable about the genetic transmission, parents still need to be well informed about it, especially on the issues like the risk concept, the meaning of the recessive inheritance and the carrier mating. Their reproductive behaviour could have been modified had they been well counselled, and social conflicts especially in the presence of consanguinity could have been avoided. Their high desire for screening would be supported by establishing genetic programmes in Kuwait, making use of the new technology in choosing preventive measures against the disease.



Dedicated to all those suffering from sickle cell anaemia

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1 Introduction

1.1. Definition

Sickle cell haemoglobinopathies result from a genetically determined, chemical alteration in the polypeptide chains of the globin portion of the molecule, by the substitution of a single amino acid at a particular point in the beta (β) chain, causing synthesis of a pathological form of haemoglobin.

Sickle cell disease (SCD) is an autosomal recessive inherited disease of serious proportions characterised by a chronic haemolytic anaemia, gradual deterioration of tissue and organ function and shortened life expectancy. [1-A,2]

The term sickle cell anaemia (SCA) is now loosely used and non specific, so the genotype description of SS disease is preferred.[1-A]

1.2. Initiation of the idea

I acquired my interest in sickle cell anaemia during my residency in the Haematology Unit at the paediatric department of Sabah Hospital in Kuwait. In the late 1970s. I was involved in the following:

- A 10 years old girl who was mentally and physically handicapped, because of vaso-occlusive crises repeatedly inflicting her central nervous system.
- A 12 years old boy, who was extremely depressed, could not cope with his school failures, repeated painful crises, and frequent admissions to hospital. He wanted to put an end to his life.

Those two patients convinced me at the time that health services offered to Sickle cell disease (SCD) patients could be extended far beyond mere treatment of painful sickle cell crises.

Ability to detect genetic diseases and screening programmes taking place in other parts of the world initiated the idea for this project.

This project was prepared and the data collected in 1990. Submission of the dissertation was deferred because of the Gulf Crisis and its consequences. The interruption of data collection by all the events of the Gulf War, reduced the original sample size to about the half. Although aware of the disadvantages of small numbers in making solid conclusions on the results, it was decided to analyse them in the same depth as previously planned. It is hoped that it will be there, and that it will be a useful stimulus for Kuwaitis to start their own genetic programmes, especially on sickle cell disease.

2 Literature Review

2.1. The abnormal molecule

In Sickle cell disease (SCD) the basic abnormality resides in the globin portion of the Haemoglobin (Hb) molecule. Hb is a conjugate of a pigment heme, and a protein, globin. The heme component consists of a protoporphyrin in combination with iron in the ferrous state. The globin component consists of two pairs of polypeptide chains, with a total of 574 amino acids per Hb molecule.[1-B] The globin portion of normal adult Hb (HbA) consists of a pair of alpha (α) chains, and a pair of beta (β) chains. In some individuals an abnormal Hb results from a genetically determined amino acid substitution in one of the polypeptide chains. Hb S ($\alpha_2 \beta_2^s$) results from the insertion of valine at position β^6 instead of the glutamic acid that occurs in HbA.[1-B] With deoxygenation the valine substitution permits abnormal polymerisation or stacking of HbS molecules, converting HbS from the sol to gel state, resulting in distortion and shortening of the life span of the RBC. Hence the phenomenon of sickled cells.

Repeated sickling produces a pattern of vascular injury in the form of intravascular cellular aggregation together with thrombosis. Although episodic, sickling can reduce the circulation and even obstruct blood vessels to impair organ and tissue function.[2] Such injuries may appear to have an errotic distribution with transient or permanent effects. Anaemic crises, painful crises, hand-foot syndrome, and the life threatening acute splenic sequestration crises are main clinical manifestations of the disease.

2.2.The Genetic Inheritance

• The total structure of each type of polypeptide chain ($\alpha,\beta,\gamma,\delta$) is determined by a pair of autosomal allelomorphic genes.[2] Many genes, particularly those coding for structural proteins rather than enzymes are known to be arranged in gene clusters, as the arrangement of the β - globin - like genes on chromosome 11, and the α - globin - like genes on chromosome 16.[6]

• Homozygous sickle cell disease (Hb SS) results from the inheritance of the sickle cell gene from both parents.[1-A] The heterozygous state (sickle cell trait) results from the inheritance of the sickle cell gene from one parent. Thus when one parent is heterozygous for the sickle cell gene and the other parent is normal, the offspring would have an equal chance of having either the sickle cell trait (AS) or a normal (A A), genotype.[1-A] If both parents have the sickle cell trait, there is a 1 in 2 chance of offspring having the sickle cell trait, and a 1in 4 chance of the offspring being normal (AA) or having SS disease.[1-A] This 1 in 4 chance of an offspring with SS disease remains for each pregnancy regardless of the result of previous pregnancies.[1-A]

• In applying Mendelian terminology to the sickle Hb genotypes, the disease is recessive in the sense that its characteristics are not manifest in heterozygotes (a benign condition), the sickle cell gene is dominant in the sense that it shows a degree of abnormality intermediate between that of the homozygote and normal.[2]

• **Other Haemogolbins in sickle cell disease:**

- Hb C: results from an amino acid substitution at the same site in the β chain as HbS, with the resultant insertion of lysine instead of glutamic acid ($\beta^{6\ glu \mapsto lys}$)$^{1\text{-}B}$.

- Hb D Punjab: glutamine replaces glutamic acid at position β^{121} ($\beta^{121\ glu \mapsto gln}$)$^{1\text{-}B}$.

- Hb O Arab: lysine replaces glutamic acid at position β^{121} ($\beta^{121\ glu \mapsto lys}$)$^{1\text{-}B}$.

- Hb E: results from the substitution of lysine for glutamic acid at position β^{26} ($\beta^{26\ glu \mapsto lys}$)$^{1\text{-}B}$.

The above abnormal haemogoblins, when inherited along with the gene for the HbS, result in clinically significant sickle cell disease.[1-B]

People with sickle cell trait Hb (AS) are not anaemic, have no physical abnormalities, are usually asymptomatic and have a normal life span.[1-C] The proportion of HbS in these people varies between 20 and 45%, the remainder being normal HbA.[1-C] However, sickle cell trait manifests many of the pathological features of sickle cell disease under unusual physiological conditions.[1-C] An example is the policy in the US Air Force excluding personnel with sickle cell trait from flight duty.[1-C]

Studies from Saudi Arabia reported HbS Heterozygotes with severe clinical manifestations, their conditions were associated with other genetic abnormalities like α-thalassaemia, β-thalassaemia and G6PD deficiency, and with iron deficiency anaemia[7].

2.3. Geographical Distribution:

- It is a common misconception that HbS is limited to the negro race, whereas it is widely distributed among non-negro peoples throughout an area which includes: Southern Italy, Sicily, Northern Greece, Southern Turkey, Palestine, the Eastern Province of Saudi Arabia (Al-Qatif and Al Hasa Oases), and India, as well as Equatorial Africa and the Americas.[1-A]
- It has been postulated that the abnormal gene arose in the Arabian peninsula (Lehman 1954) and reached Africa through a land bridge which was used to connect these two continents in the distant past.[8] The single Mutation Theory.[1-D]
- Recently, the Multiple Mutation Theory has received support from studies of DNA polymorphisms. Geographical studies of linkage pattern have linked

the West African origin of Americans' β^S gene, and have linked the β^S gene of Gabon with that of the Ivory Coast, Kenya, Saudi Arabia and India.[1-D]

• In a geographical survey of β^S - Globin Gene Haplotypes (1986),[9] chromosomes of individuals from Nigeria and from the south west of the Arabian Peninsula had the haplotypes previously found in West African, Jamaican and USA blacks, whereas those from the Eastern Oases of Saudi Arabia and from the west and east coast of India showed a different haplotype not found in Africa.[9] This data was taken as evidence for an independent Asian origin of the sickle cell mutation.[9]

2.4. Sickle cell disease in Kuwait

• Reports about SCD in Kuwait have been very few. Ali (1970) reported the presence of a milder variant of the disease in Arabs in Kuwait and noted unusually high F Hb in two families.[10] Later, similar reports about the mild SCD came from Saudi Arabia (Perrine 1972)[11] and from Kuwait.[4,12]

• Although the African SCD is more severe compared to the disease in Kuwait, both are similar in the definite relationship between the occurrence of painful crises and meteorological changes.[13] The rise in incidence of crises occurred during the extremes of weather in both the hottest and the coldest seasons.[13]

• Though a proper survey of the incidence of the HbS gene in the Arab population in Kuwait has not yet been undertaken, Ali showed that the number of cases of HbS encountered during routine investigations in the haematology section in 1967 and 1968 were 48/2680 and 51/2481, i.e. 1.8% and 2% respectively.

• As the incidence of SCD has been related to the degree of endemicity of malaria in Africa[1-B] and in Saudi Arabia,[3] Kuwait has not been a malaria endemic country.

"Despite William Shakespeare's axiomatic statement (What's past is prologue), history cannot be considered a predictive science".[14] It remains necessary to determine the public health implications of the high prevalence of SCD there.

2.5. SCD in Saudi Arabia

• Lehmann showed in 1963 that the presence of sickle gene in the Eastern Province (AL-Qatif and AL-Hasa Oases) was 25.1% amongst Shi'i, while it was 10.2% amongst Sunni of the same province. Other provinces (west and central) had a frequency of 1%[3]. The distribution of HbS gene was related at least in part, to the recent malarial history of the population.[3]

• Based on the observations in the Eastern province only, it has been stated that the average clinical course of the disease in Saudi Arabia is much more benign when compared with that in USA or Caribbean Island, with rare death in early childhood, with delayed splenic atrophy and less susceptibility to infection.[15]

• Recently it has been shown that sickle cell anaemia (SCA) in Western and south-western population of Saudi Arabia, is as severe as is described in American blacks, with recommendation of penicillin prophylaxis to SCA children in those regions of the country.[16]

• Two variables are well documented modifiers of the sickle cell phenotype, the level of HbF production[17] and α thalassaemia.[18,19] Both are particularly relevant to Saudi Arabia.[5,18,20] Pembrey postulated in 1978 that the unusually elevated levels of Hb F in the Oases of eastern Saudi Arabia are from a genetically determined absolute increase in HbF production related in some way to the SS genotype.[21]

• Recently it has been shown that Faetal haemoglobin levels in SCD and normal individuals are partially controlled by an x-linked gene located at $xp_{22.2}$.[22] F-cell

levels were significantly higher in non anaemic females than males, and F-cell production as determined by F reticulocytes levels was higher in SS females than in SS males.[22]

• Although studies from Saudi Arabia described the distribution of HbS gene,[3] the HbF and the benign disease,[15,21] the prevalence of haemoglobinopathies,[5] the interaction of other genetic disorders and the clinical course of the disease,[20,23] there is hardly any study which described or discussed the genetic counselling implications, families knowledge and their perception of the disease, or their attitudes to screening.

2.6. Other parts in the Middle East: e.g. Jordan

A family case report of sickle cell - thalassaemia,[24] and the fact that this study includes 7(13.5%) Palestinian - Jordanian families, show that SCD does exist there.

2.7. SCD in the UK

• There are more than 5000 individuals with SCD in the UK, making it the commonest genetic disorder in many inner city areas of the country. [25] It is carried by 10% of Afro-Caribbean people in the UK, most of whom had emigrated from the West Indies.[25]

• In a survey in England and Wales, 1367 cases of SCD were identified; 862 were in London.[26] The Brent sickle cell register which started in 1979 contained 184 patients until 1984.[26] "The incidence of SCD in Britain is increasing because of the babies born every year to parents of Afro-Caribbean origin".[26] In another review of Brent register (1989) it was found that while 30% were a result of new diagnosis, the majority of additions had resulted from

demographic changes, with the highest number being temporary visits from Africa.[27]

• The prevalence per 1000 births in Brent in 1984 was 1.6 for SS and 0.3 for S/β^+thal,[26] while in Jamaica it was 3.1 for SS and 0.34 for S/β^+thal.[26] The carrier rate (AS) in 1984 was 2.8% of all births at Brent, while it was 10% in Jamaica.[26] It was also estimated that between 50 and 100 babies with SCD may be born in London alone every year.[26] In Brent nearly 40% of all acute admissions to haematology beds are for acute sickle cell disease manifestations.[26]

• In Birmingham, all new born babies are tested by haemogoblin electrophoresis at the same time as they are screened for hypothyroid and phenylketonuria.[25] Parents of affected babies are given appropriate advice. Their children are followed up in a paediatric haemoglobinopathy clinic.[25]

• A 10 year clinical study in Birmingham, where the majority of black population is of West Indian origin,[28] suggested that the environmental differences between temperate industrial Birmingham and tropical rural Jamaica had influenced the clinical manifestations, in terms of less sever infections and more pulmonary and anaemic crisis.[28] Birmingham's annual mortality rate was 1.3% for SS and occurred in children under 3 years, while 87% of SS Jamaican study survived the first two years of life.[28] The influence of environment on differences in the frequency and presentations of SCD between tropical Africans and their counterparts in Europe was also noted elsewhere.[27]

2.8. Neonatal screening

• Neonatal screening programmes are now an established and effective method for the diagnosis of SCD with automation of the various techniques.

Newborn screening for SCD and other haemoglobinopathies has been advocated for several years.[29] Such programmes were initiated in the UK and

USA in the early 1980s.[27,30] A higher incidence than might have been expected has been diagnosed in some centres,[27,31,32] while others prospectively reported no deaths over a period of 8-20 months in infants with SCD diagnosed neonatally.[33]

• Comparison of the outcome between infants who were followed prospectively since their diagnosis at birth, and those whose mothers were contacted 2-4 years after the birth of a child with a positive newborn screening; it was shown that screening significantly reduced mortality, and increased parental awareness of complications, and thus improved the prognosis.[34] In a retrospective study to assess care of children with SCD, half of infants diagnosed neonatally had not been followed up.[30] "Neonatal screening must be linked with follow up to ensure optimal management".[30]

• A study from Colorado reviewed the results of newborn screening performed on dried capillary blood spots.[35] The results confirmed the value of newborn screening for haemoglobinopathies but suggested a more sensitive test.[35] The initial screening failed to detect SCD in 4 infants among 528711.[35] While delayed diagnosis occurred in infants somewhere else, at a mean age of 215 days, for failure of directly contacting the parents of the positive newborn screening results.[36]

• Though newborn screening has been recommended for all infants,[37] it is concluded in a cost-effectiveness study that screening black infants is very worthwhile, but screening populations in which the haemoglobin S gene is rare is unjustified.[38]

• In a recent study, RNA was extracted from newborn screening dried blood specimens. The method successfully distinguished beta A and beta S transcripts in unaffected (AA), carrier (AS), and affected (SS) individuals,[39] it was also valuable in identifying a compound heterozygous patient with S/beta-thal.[39]

2.9. Prenatal Diagnosis

• Sickle cell trait had been identified by the study of blood obtained after abortion.[40]

• Prenatal diagnosis for SCD was first introduced in 1975.[41] Foetal blood obtained by placental aspiration at 22nd week gestation[42], diagnosed the homozygous state of SCD in utero. However, a foetal loss of about 5% due to these invasive procedures[43] provided the impetus for improved techniques using DNA analysis of amniotic fluid cells[43,44,45,46] by amniocentesis at 14-16 weeks gestation.[46,47] Chorionic villus sampling has permitted diagnosis in the first trimester of pregnancy usually at 6-8 weeks of gestation.[46,47] Coloured DNA amplification was reported as a rapid method for prenatal diagnosis.[48]

• In 1990 it was demonstrated that nucleated cells are present in maternal blood during pregnancy.[49] Molecular diagnosis of Hb Lepore - Boston in the foetus was accomplished using peripheral maternal blood as a source for foetal cells at 8th to 10th week of gestation.[49] This was a demonstration that prenatal diagnosis of a genetic disease may be feasible without invasive procedures.[49]

• "Such early diagnosis allows an informed decision on continuing the pregnancy or requesting selective abortion of an affected foetus".[47] On parents' request termination of pregnancy was performed.[47,50] Although it was reported that the uptake of prenatal diagnosis is very much higher in families with one severely affected child,[25] many prospective parents choose to take the choice that their child may not be severely affected.[25]

• Identification of couples at risk of having an affected child is necessary for establishing an antenatal diagnostic programme.[47] Such couples have their right in a well informed genetic counselling,[51] which "helps to identify parents who hold strong and clear views on the necessity of prenatal diagnosis".[51] The genetics programme of Cuba is an example for prevention of SCD.[52] Couples' decision on taking the choice of prenatal diagnosis[44] and therefore of

termination of pregnancy is influenced by the quality or the lack of previous information, the experience with the condition, and the religious or moral principles.[47,51] However, avoiding stigmatization of an ethnic minority is necessary in any genetic programme.[14]

• Recently (1993) using buccal cell analysis, it was shown that pre-implantation diagnosis at the 8-cell embryo stage could be carried out safely and reliably for a couple at risk of transmitting SCD to their children.[53]

2.10. Knowledge, attitude, coping and counselling in genetically determined diseases

• **SCD**

In a Jamaican study, both female patients and the mothers of patients with SCD recognised that early diagnosis is important to the management of the disease. The majority preferred antenatal diagnosis (58% of patients and 76% of mothers) and these voted in favour of the first trimester procedure.[47] Faced with the diagnosis of a foetus with SS disease, 30% of patients and 46% of mothers stated they would request termination.[47]

In a Cuban programme for prevention of SCD (1983-89), 531 (65% of at risk) couples elected to have prenatal diagnosis, 98 affected foetuses were found. In 72 cases the pregnancy terminated.[52] During operation of this control programme, the expected 100 children born annually with SCD was reduced to about 30%.[52] The Cuban prospective aim was to increase the level of knowledge about the disease in the whole population.[52]

Increased knowledge and awareness about SCD among Black Americans has not resulted in a widely held pool of accurate and meaningful information, upon which families and youths build up their decisions. Meaningful knowledge about SCD is vested within a network of religious, civic, fraternal and social organizations of a community.[54]

It was demonstrated that the use of oral penicillin prophylaxis is highly effective in reducing the risk of pneumococcal sepsis in children with SCD,[55] therefore decreasing their mortalities.[56] The need for more comprehensive education of the parents of these children was emphasized to ensure compliance with penicillin administration.[57]

• Bone marrow transplantation was performed on 12 patients aged 11 months - 23 years, all patients are alive and well. With follow up ranging from 9 -51 months, a complete cessation of vaso-occlusive episodes and haemolysis was observed and a change in Hb pattern in accordance with the donor's electrophoretic pattern.[58]

• In spite of the 15% mortality risk,[59] a substantial minority of the parents of children with SCD may consent to bone marrow transplantation for their children.[59] Their decisions were not related to the clinical severity of their children's illness.[59]

• Pain coping strategies in SCD children and adolescents and their parents were assessed. It was found that parents high on coping attempts had children who were more active and required less frequent health care services. While children high on negative thinking and passive adherence were less active, required more health care services and were more psychologically distressed during painful episodes.[60]

•"The genetic origin of SCD makes it essential that a psychological understanding of the disorder should be a component of the therapy arsenal of health professionals serving populations of African extraction".[61] Psychiatric morbidity, antisocial behaviour, neurosis and other behavioural problems among SCD patients were discussed.[62]

• **Thalassaemia major:**

Direct involvement of the community seems to be of maximum importance for the success of a genetic disease prevention programme.[63] For example, the birth rate of children affected by β-thalassaemia major has fallen by 96% in

Cyprus, by 90% and 62% in the Italian provinces of Ferrara and Sardinia respectively, and by over 52% in Greece.[63,64,65] The Lombardy Region programme in Italy resulted in a decrease ranging from 30% to 50% in the birthrate of children with β thalassemia major.[63] The programme consisted mainly of parents' associations participation, spreading knowledge in the community, genetic counselling and prenatal diagnosis.[63]

The effect of antenatal diagnosis on the reproductive behaviour of families at risk of thalassaemia major was reported by Modell (1980).[66] 94% of British Cypriot communities requested antenatal diagnosis, whereas only 59% of the Indian and Pakistani communities requested it, which reflects differences in cultural beliefs and level of awareness.[66]

- **Cystic Fibrosis:**

Studying effects of newborn screening of cystic fibrosis on maternal behaviour indicated that newborn screening had not increased a mother's tendency to overprotect her child with cystic fibrosis and in some cases the tendency had decreased.[67] Delay in diagnosis when screening was not conducted usually caused mothers considerable personal distress.[67]

Carrier identification of those at risk for an inherited disease is a precondition for effective programmes offering genetic counselling and prenatal diagnosis. In a community study about cystic fibrosis there was only a limited knowledge of the disease,[68] and over 80% of those who had heard of it stated they would wish to know whether or not they were carriers.[68] In a study which included families with a cystic fibrosis child, a majority wished to have the opportunity of prenatal diagnosis, although not necessarily to use the information to terminate affected pregnancies.[69]

- In another community survey about cystic fibrosis, 58% of those who had contact with the disease knew it could only be inherited, compared with 40% of those who had no reported contact.[70] Three quarters of the respondents

accepted the idea of carrier testing for themselves, and all considered that testing should be available to those planning a family.[70]

• **Duchenne Muscular Dystrophy:**

Although Duchenne muscular dystrophy is an untreatable condition, the majority of mothers said that they would opt for neonatal screening.[71] The main reason for having the screening test was to prevent the birth of further affected babies in the family.[71]

• **Chorionic Villus Sampling (CVS):**

Mothers' attitudes following CVS for prenatal diagnosis were encouraging.[72] 93% reported CVS to be a satisfactory procedure and thought earlier diagnosis was beneficial. 81% reported a better experience with CVS than with a previous amniocentesis. 93% wished a CVS in a future pregnancy and 97% would accept a risk of miscarriage from the procedure of twice that quoted for amniocentesis.[72]

• Genetic counselling which must respect cultural, social, religious and economic factors of an affected community was well emphasized by Anionwu.[51] Disclosing genetic information by doctors to a third party where it is in the medical interest of that third party to know genetic information is an ethical dilemma.[73]

3 Hypothesis

Recently in Kuwait, there have been trials to establish neonatal screening programmes for some genetically determined diseases. Unfortunately none of those programmes came to a successful conclusion.

Before establishing any screening programme, it is crucial to determine the views of local people, given their present standard of education and modernisation. Do they for example accept screening and when? Or do they want to rely on custom and religion?

Sickle cell anaemia being a frequent trait in the Arabian Peninsula[3,4,5] is taken as an example of a genetically determined disease, which is at the same time suitable for screening prenatally and / or neonatally.

Educational aspects of such a screening programme design are an essential component of successful operation.

The following are all necessary features of a successful screening programme:

- Adequate knowledge and counselling should be offered to parents identified as having children with sickle cell disease (SCD) or trait.
- When such diagnostic information is offered, subjects should be able to understand it and plan their life accordingly.
- Having gained knowledge about the disease, this knowledge has to be absorbed into their general cultural views and habits. Also they need to cooperate effectively in the use of a screening programme.
- The screening programme itself should be well designed to serve parents or possible parents known to be liable and the population in general.

My hypothesis is that in the absence of a genetic programme in Kuwait prior to 1990, especially for SCD, affected families could not opt for better choices in planning their families and their future life. Their conditions could have been made better given a programme which meets the above criteria and the resources available.

4 Objectives

In this context I attempted to:

• Enquire into the quality of knowledge about genetic transmission of the disease among parents of (SCD) patients.

• To describe their social and reproductive behaviour, in the presence of this inherited disease in their families.

• To ascertain their attitudes towards screening, prenatally, at birth and later on, and to question their response to termination of an affected foetus.

Paediatric Department of Sabah Hospital - Kuwait (outside)

Paediatric Department of Sabah Hospital - Kuwait (inside)

5 Methods of study

The following methodology was adopted to enquire into the standard of knowledge among parents of SCD patients, and into their attitudes towards screening.

5.1. Type of study

A cross sectional study, which aimed to determine and analyse families' views about SCD in a certain time.

5.2. Setting

It was conducted in the Haematology Unit of the Paediatric Department of Sabah Hospital in Kuwait, which treats patients with Haematological diseases from all over the country.

Refer to appendix 2 for a more detailed review of Kuwait.

5.3 Time of study

Time allocated for this field project of the MSc in MCH, was July and August 1990. The first week of July 1990 was an Eid holiday (a Muslim Religious Festival). The second week and a half were consumed in obtaining an ethical agreement and in opening channels for the project. Interviews took place in the last week and a half of July 1990.

The project was unfortunately seriously interrupted on 2nd August 1990 by the events of the Gulf Crisis. In such circumstances, the project could not be completed as had originally been planned. The end of war was on 26 February 1991. But it was not until August 1991, that the project could be irregularly resumed. The return of Kuwaitis and exit of non-Kuwaitis occurred on a large scale. The post war situation was most unsuitable for such a project to thrive.

Data collection had to be abandoned in October 1991. Fortunately a sufficient number of observations (52) were collected to make some conclusions possible.

5.4 Definition of cases

Initially 110 families were included in the study, being all those whose records documented the presence of at least one SCD Homozygous child. Patients were said to have SCD - Homozygotes - if Hb (SS) had been diagnosed on Hb electrophoresis.

Patients were only included in the study if they were still alive at the time of interviewing their parents. In order to generate a good sample size, patients who were born between 1968 and 1986 were included in the study.

5.5 Sample size and selection of cases

All the steps of the project, including cases identification, recruitment and interviewing were done by me. No team was assigned to assist in data collection and no support of any kind was provided.

5.5.1. Patients' records

Records of SCD patients were among many other patients' records of different haematological diseases. An office was allocated for these records under the care of the Unit's secretary. Updated notes are routinely recorded about patients' conditions as well as results of investigations and management. Other standard hospital files were used for admitting patients to the hospital, and for regular service, but these contained no additional information useful to this study.

The access to the files was not easy. SCD patients were not on regular follow up. They appeared only when they needed medical attention. A meticulous effort was required to identify records of SCD patients, and to separate them from thalassaemias, leukaemias and other blood diseases.

5.5.2. Number of recorded SCD patients

The total number of SCD and trait patients was: 210. 159 (75.7%) were Kuwaitis and 51 (24.3%) were non-Kuwaiti Arabs and other Muslims. 140 (66.7%) were Homozygotes, and 70 (33.3%) were Heterozygotes. They were children and adolescents of 144 couples, with a mean of 1.5 per couple.

5.5.3. Accessible Parents

34 families were unreachable because of absence of addresses and telephone numbers, or lack of updating of the same. The total number of accessible couples was 110 = 76.4% of the total recorded number. Those it was possible to contact, were willing to co-operate and promptly to a remarkable extent.

5.5.4. Organisation of patients and their parents

Patients were organised according to the year of opening the file in the haematological unit, starting by 1990 - 89 and ending by 1970s (see table 1).

Table 1 Organisation of accessible patients and their parents according to the year of opening the file, before and after the Gulf Crisis.

Year	90-89	88	87	86	85	84	83	82	81	80	70s	Total
Number of families accessible before the Gulf Crisis	7	4	4	11	7	5	12	6	14	7	33	110
Number of patients accessible before the Gulf Crisis	8	4	5	14	9	7	15	7	22	13	57	161
Total number of accessible families after the Gulf Crisis	7	3	3	10	4	5	9	4	7	3	10	65
Number of recruited families	7	3	2	10	2	5	7	4	3	3	6	52

5.5.5. The goal of sample size

Because of the limited number of recorded accessible families, it was decided to study all the 110 families.

5.5.6. Reduced sample size

Because of the events of the Gulf War, 45 families became inaccessible. They had left the country or had changed their houses. The total sample size was reduced to 65.

5.5.7. Recruited patients

a) 40 families were recruited and studied before the Gulf Crisis, between 20th July and 1st August 1990.

b) 12 families were recruited and studied after the Gulf Crisis, during August and September 1991. The process took much more time in Post - War Kuwait.

5.6. Technique of the study

This study was performed by interviewing parents of affected children using a structured questionnaire, the proforma of which is attached in appendix (1).

The investigator, approached parents by telephone. They were asked to collaborate, and both parents or one of them responded. Care was taken to involve both parents at the interview as far as possible.

Interviewing parents in their houses takes more time, because families did not appreciate a home visit and tended to postpone it. Their customs of hospitality and kindness to their guests, would add to the length of time taken. Therefore all parents were called and interviewed at the haematology unit, which makes it a truly representative unbiased sample.

After the format interviews, I sat with the parent/s and talked with them about the disease and its genetic implications. This was to lay the ground for further prospects in future studies of the disease. I thought of re-evaluating the same

families' knowledge about the genetic transmission of SCD, and to find out whether they have changed their social and reproductive behaviours and attitudes. This intervention built up a good relationship between the families and the investigator. All interviews and conversations had to respect the local thoughts and habits in the Middle East.

5.7. The Questionnaire

This questionnaire comprised multiple choice questions as well as open ended questions, to allow the families to express their opinions as accurately as possible. It was developed by considered 'apriori' in the literature review.

There were 10 questions to test the parents' knowledge about genetic transmission of the disease; 11 to ascertain their attitudes towards screening and towards transmission of information about genetic risk within the family; 7 to evaluate the reproductive behaviour after diagnosis of the affected child; 9 to question their perception of the disease and its impact. 10 questions related to sources of their knowledge, and 13 questions to identifying characteristics of the parents and the index patient.

The interview started by a keen enquiry about the index patient. Questions about the parents' characteristics were asked at the end of the interview.

The investigator thought that the questionnaire was long, but parents were interested, they expressed their anxieties and worries and volunteered to give more informations which were not on the questionnaire, especially those related to their social and psychological agony of the disease.

5.8. Pilot study

A small pilot study was conducted to overcome any constraints and problems, and to correct any ambiguity in the questionnaire and ensure that useful information was obtainable from the study. 6 families were interviewed. Their children were admitted to hospital because of sickling vaso-occlusive crises, or for blood transfusion.

The outcome of this initial piloting:

a. Obtaining date of birth of other children: mothers/parents were not comfortable about surrendering Birth Certificates of their children. Thus, when they were approached by phone calls, they were asked to recall birth dates of their children, and the investigator relied upon their memory.

b. Some of the questionnaires were modified; e.g. the rather difficult questions which ask for the parents' responses to termination if the prenatal diagnoses were positive, and which test their knowledge about the chances of having an affected child.

c. Diagnosis and year of opening patient's file were indicated on the questionnaire.

5.9. Final study:

The final study commenced on 20th July 1990. 40 families were studied before the eruption of the Gulf Crisis on 2nd August 1990. Considering summer holidays when many people are abroad, the numbers are good.

Each day the investigator called people by telephone. They responded readily. They appeared on the same day, 3 or 4 hours after the call, or the next day. Many of them expressed their appreciation for considering their participation and their opinion on the project.

Interviewing a Kuwaiti mother

The average duration of the interview was 60 minutes, and of the intervention 45 minutes. In many instances, a cup of tea was offered in the middle of the session. On average, 4 families were interviewed each day.

The "Brent Sickle Cell Leaflet" was translated by me into Arabic (appendix 3). Because of delay in obtaining an agreement from Brent Centre and from local authorities to distribute the leaflet on interviewed parents, it was replaced by an explanatory session. The meaning of the disease and trait, the recessive mode of inheritance, the chances of having a carrier or an affected child were explained after each interview. Parents' questions were answered as well.

The study was resumed several months after the end of the Gulf War, using the same technique. But the circumstances were different, and parents did not show such a ready response. Only 12 families were studied.

5.10. Limitations of the study

The desired number of families could not be studied because of the following limitations:

a) July 1990 could have been made more useful if ethical agreement and arrangements for the project were fulfilled earlier.

b) Weather, summer holidays and Eid: July and August are the hottest months in Kuwait (temperature 48 - 50°C). Many people were abroad on their summer holidays and were expected to return in August. In many instances, it was a grand parent or a maid who answered the phone call and asked to call again in August when the parents would be at home. Eid holiday was another factor. During Eid people observe Islamic customs and enjoy family gathering.

c) Interviews were done mostly in the afternoons, because mothers were busy before noon with their household responsibilities and fathers with their jobs. Afternoons were also more convenient, because the Haematology Unit

was very busy before noon, and colleagues were not so comfortable with the project activities done before noon.

d) The Gulf crisis

The project was interrupted on 2nd August 1990 by the Gulf crisis and the subsequent events of war, during which it was impossible to do any activity on the project. Many people left the country, mainly non - Kuwaiti Arabs. The population was reduced to about half * and its construction was changed.

People changed their addresses because of the damage or seeking for less expensive rents. The "Post traumatic stress syndrome" affected some people and reduced their enthusiasm. There was a multitude of political problems far too many to mention in detail.

5.11. Response rate:

Two families did not respond before the Gulf Crisis, and 8 after the crisis, resulting in a response rate of 80%.

Three patients (4.6% of accessible families) were not alive at the start of the project. Information which was obtained only by calling their families. Their parents were not called for interview. Approximately a 15.4% non-response rate was seen immediately after the Gulf Crisis. People did not directly refuse to participate. They gave various reasons, for example:

- *"We are busy this week, contact us later".*
- *" I am not in the mood to talk about it. I have to reconstruct my house".*
- *"My mum says she is not here now".*
- *"Give us a chance two days later". Then further excuses were given via the children in the house.*
- *" I am not well, and I have to stay with my children".*

* No new census is available till now. The source is what has been mentioned in the press and the news , via official channels.

5.12. Data analysis

No computer facilities were available in the post war at the end of the project in Kuwait. All calculations were undertaken manually, using a scientific calculator. simple statistical tests were used; sum, mean, percentage and standard deviation. Because of the small numbers, no other tests could be used.

6 Results

In this chapter results could not be always conclusive, because of the small numbers.

6.1. Studied families and their index children:

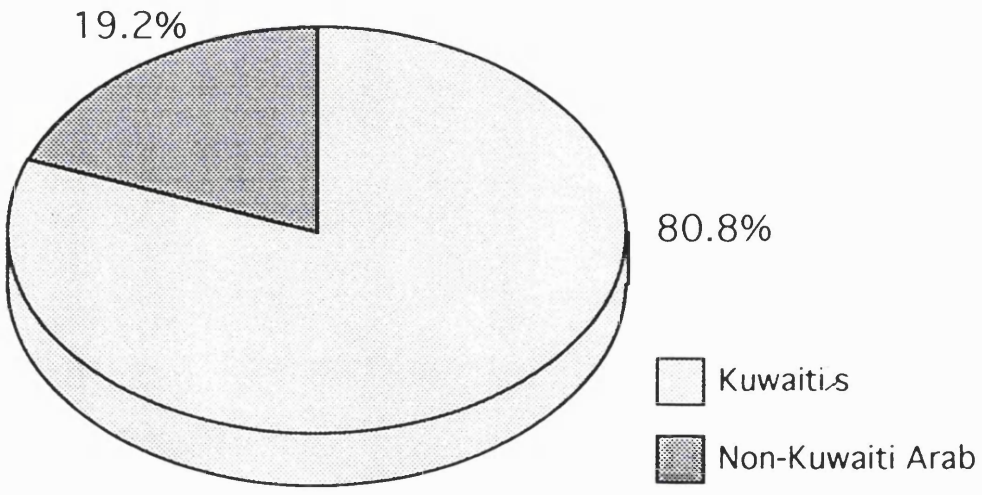
Total number of families studied : 52

Parents of these families had 261 children, mean: 5, among whom 124 were identified by blood testing (which did not include all of these children) as having HB S. 82 (66%) were Homozygous, and 62 (34%) were Heterozygous.

Each family had at least one homozygous child.

Index children (N = 52) were those children whose names were on medical files in the Haematology Unit, thus helped to trace the families.

Figure No 1 Nationalities of studied families



a. Characteristics of parents:

N = 70. Responded as : 18 (51.4%) couples, 26 (37.2%) mothers, and 8 (11.4%) fathers.

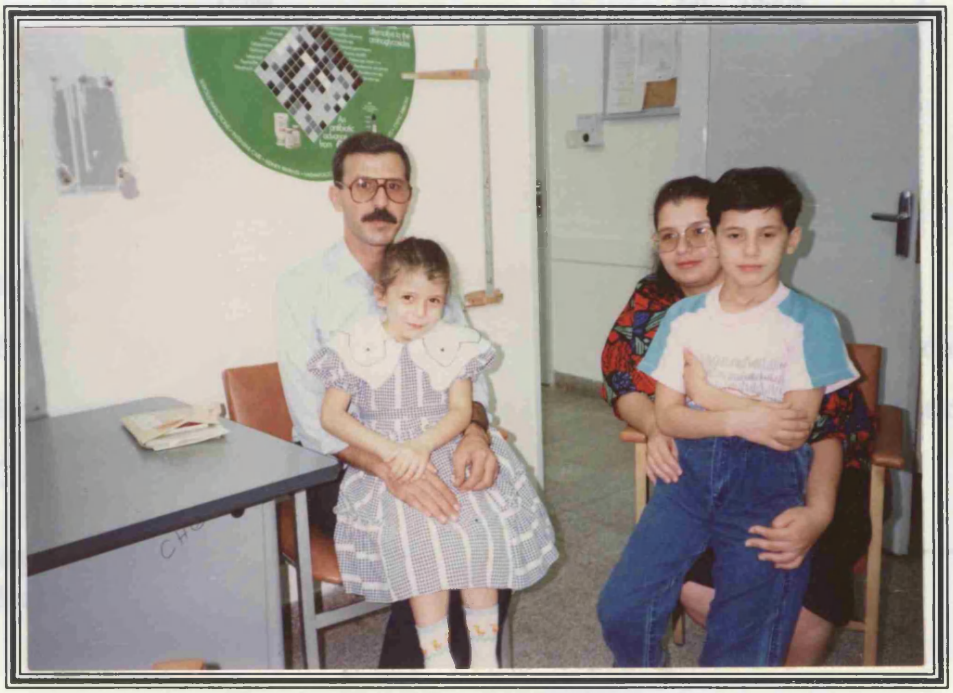
42 (80.8%) were Kuwaitis, and 10 (19.2%) were non-Kuwaiti Arabs, 7 (13.5%) of whom were Palestinians, 2 (3.8%) were Lebanese, and 1 (1.9%) was Iraqi.

In order to overcome the absence of definite classification of socio-economic classes in Kuwait, information about parents' education and family income was collected. As decisions on family planning and organisation are made by both mother and father, one influenced by the other, education of both was identified, whether the interview was given by one or both.

Percentage of standard of education among "above 10 years" Kuwaiti population, females and males, is shown in the table 2.[74] Although (SCD) families are not expected to be representative of the total population of Kuwait because of their selective character, some resemblance is noticed.

Each family father's nationality was collected. However, in all studied families, fathers were married to women of the same nationality.

A mother (right) at the intervention session.



An interviewed non - Kuwaiti Arab family

Table: 2 Characteristics of parent

•Parents (N = 70)		N	%	
Mother		44	63	
Father		26	37	
•Age / year	Range	Mean	SD	
Mother	(24-55)	37.5	7.7	
Father	(27-51)	38.7	6.6	
		N	%	
• Nationality				
Kuwaitis		(42)	80.8	
Non - Kuwaiti Arabs		(10)	19.2	
• Consanguinity		N	%	
Consanguineous (1st cousin)		32 (16)	61.6 (30.8)	
Non - Consanguinineous		20	38.4	
• Education				
Mothers (N 52)		N	%	Census 1989[74]
College+		12	23.1	12.8%
High School		9	17.3	10.4%
Primary School		21	40.4	46.3%
None		10	19.2	30.5%
Fathers (N 52)				
College+		15	28.9	14.1%
High School		10	19.2	13.7%
Primary School		22	42.3	54%
None		5	9.6	18.2%
• Family Income* - in thousand KD/year			N	%
		20 - 35	4	7.6
		10 - 20	28	54
		3.5 - 10	15	29
		< 3.5	5	9.4

b. Characteristics of index children

Fifty two index children entered the study, 46 (88.5%) of whom were Homozygous, (SS), and 6 (11.5%) were Heterozygous (AS), but had affected (SS) siblings. With a male/female ratio of 1.36/1.

* Family income as ascertained befor the Gulf Crisis.
Exchange rate 1 Kuwaiti Dinar (KD) = £ 2.

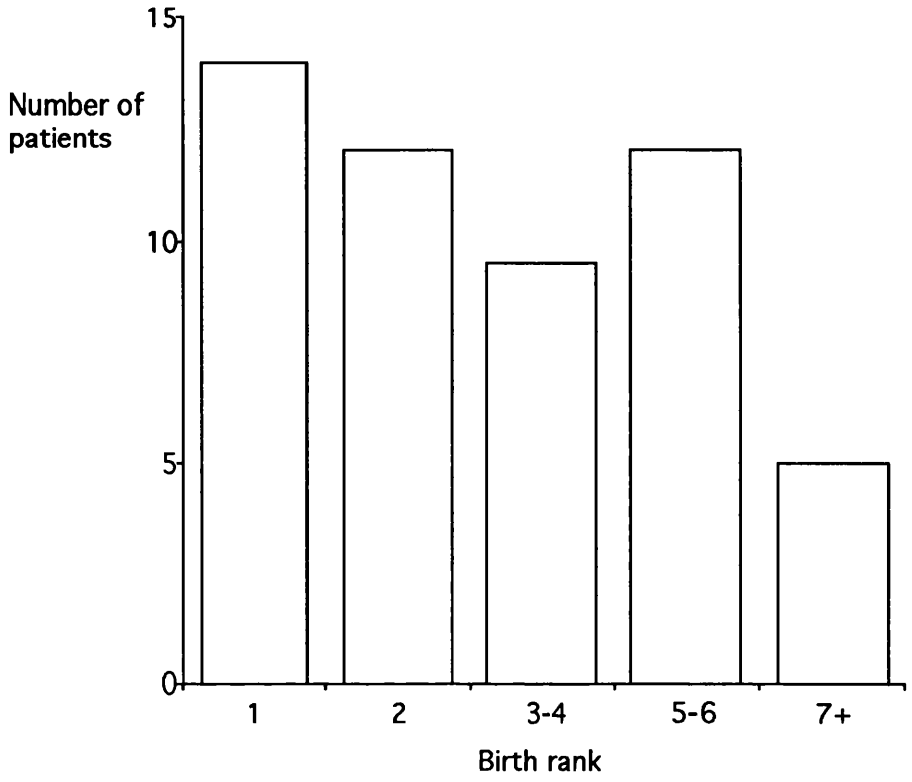
Male predominance was noticed in other studies of Sickle CSD patients.[7,23] Their ages ranged between 4 and 22 years.

• **The Birth Rank:** The index child was the first born in 27% of families, the second in 23% of cases, the 3rd or 4th in 17.3%, the 5th or 6th in 23%, and the 7th to the 11th in 9.7% of families figure 2.

Table 3 **Characteristics of index children (N =52)**

	N	%
Genotype		
Homozygous	46	88.5
Heterozygous	6	11.5
Sex: Male	30	57.7
Female	22	42.3
Birth rank		
1	14	27
2	12	23
3 - 4	9	17.3
5 - 6	12	23
7+	5	9.7
Age		
Range	4 -	22 years
Mean	10.4	(SD 4.9)
Age groups/year		
< 5	4	7.7
5 - 9	18	34.6
10 -14	19	36.5
15+	11	21.2
Age at onset: of symptoms		
/Months: 2- 6	7	13.4
6-12	9	17.3
/years		
1-2	13	25
3-5	15	29
8-6	5	9.6
No sympt. + dont know	3	5.7
Age at diagn./year (Range 3 mths-10y		
< 1	9	17.3
1 - 2	20	38.5
3 - 5	16	30.7
6 - 10	7	13.5

Figure No 2 Birth rank of studied patients



• **Age at diagnosis and length of time suffered before diagnosis**

The earliest age at diagnosis was 2 months, and the latest was 10 years. SS disease does not usually become apparent in the first six months of life, although documented symptomatic disease as early as one to three months has been described.[75]

9 (17.3%) were diagnosed before the age of 1 year, and 43 (82.7%) were diagnosed between 1 and 10 years of age.

25 (48%) patients suffered before diagnosis. Range of time was between 1 month and 9 years, with a mean of 20 months (SD: 23.3).

25 (48%) did not suffer before diagnosis; 7 (13.4%) of whom were diagnosed 6 months to 4 years earlier than onset of their symptoms. They were diagnosed when family screening was performed after the diagnosis of another member of the family, or incidentally when blood samples were collected for other purposes. 18 (34.6%) were diagnosed at the time of onset of symptoms.

• **Admission to hospital:**

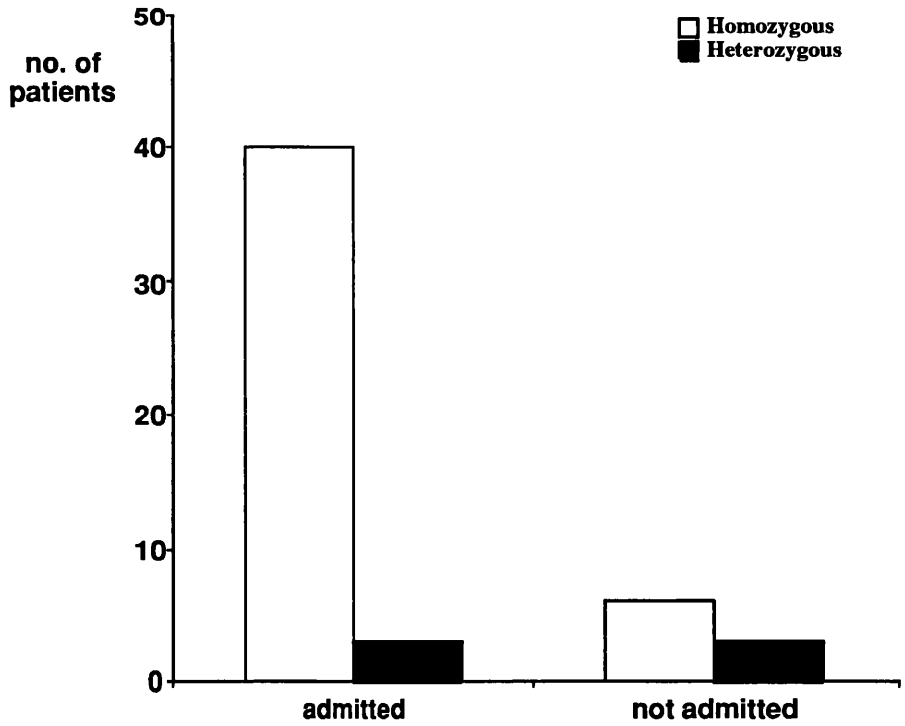
43 (83%) of patients were admitted to hospital because of SCD symptoms, 3 of whom were heterozygous, which coincides with others' observations in the Arabian Peninsula.[7] 9 (17%) were not admitted, 6 of whom were homozygous, which coincides with others' description of the benign Arabian variety of SCD.[10,11.76]

21 (40.4%) of patients were admitted to hospital because of other reasons than SCD symptoms, and 31 (59.6%) were not admitted.

Mean age at first admission was 3-4 years (SD: 2.1)

Frequency of admission of 28 (54%) was every 1-6 months, and of 15 (29%) was every 1 year or less.

Figure No 3 Admission of index patients to hospital



• **Deceased children:**

14 (27%) families had children who died, 7 (13.5%) of whom, the death was related to diagnosis. While Pearson and Al Rasheed (1987 in Kuwait) documented only one death from causes unrelated to SCD in their study.[4]

6.2. Parents knowledge about SCD genetic transmission

6.2.1. Perception of the disease:

45 (87%) of families thought that the disease is serious, and 7 (13%) thought that the disease is not serious.

Table 4

Reasons why respondents thought the disease is serious

Reasons	%
• Uncertainty about the future	42
• The affected child is almost always ill	42
• Frequent admissions	38
• Not growing well	7
• All the above	27

• The numbers are not mutually exclusive, because respondents were allowed more than one choice.

This question gave an opportunity to many of the parents to express their anxieties, their feelings of uncertainties, and their requirements for more than one usual medical support.

Although some families perceived their children as "not growing well" (table 4), growth was not documented in any of the patients' medical records.

Those who thought the disease is not serious (N = 7) : their affected children were not admitted to hospital (N = 3), or were admitted only once (N = 4). Children of 5 of these families were diagnosed 6 months to 4 years earlier than the onset of their symptoms or at the time of onset.

Studies about the Arabian variant of SCD described the clinical nature of the disease[4,7,10,11,76] but did not question families' perception about it.

- **Scoring of knowledge:**

Each parent/s were asked a series of questions (N = 10) to assess the extent of their knowledge. An index of overall knowledge was constructed by giving a score of 1 for each correct answer. Those who scored 8-10 out of 10 were graded as "good", 6-7 out of 10 were graded as "fair", and 5 or less were graded as "low".

- **Knowledge distribution amongst the families:**

6.2.2. SCD aetiology:

Families' knowledge about the cause of the disease was good. 47 (90.4%) knew that it is caused by an inherited factor. The numbers are raised to 50 (96%) when they were asked whether they had been told that SCD is caused by an inherited factor. Only 3 (5.6%) thought that the cause is an unknown factor and 2 (4%) thought that it is caused by an illness in the mother during pregnancy, or because the child is not eating well.

6.2.3. Understanding the recessive transmission of the disease:

Parents who knew that SCD is caused by an inherited factor were asked about its transmission. The consequences of a mating of two gene carriers were fairly well known, 31 (59%) families knew that it is transmitted from both parents.

Table 5

Families' understanding the recessive transmission

Transmission	Number	% of sample N = 47	% of population N = 52
• From both parents	31	66	59
• From father alone	6	12	11
• From mother alone	5	11	10
• Neither from mother nor father	5	11	10

Those whose answer was neither from mother nor father thought that it runs in the family by chance, or they accepted what was told to them, without having the concept on the meaning of inheritance. This evolved when they argued about it at the session of "intervention":

"Yes, it is inherited, but it is my aunt's daughter who is affected, it is not me".

In a study conducted on parents of cystic fibrosis patients, another autosomal recessive inherited disease, 97% of families understood this concept clearly.[77]

6.2.4. Knowledge about the carrier state:

36 (70%) families were aware that some of their children are able to transmit the disease to their own children, 7 of whom (19.4% = 13.5% of total population) thought that such a carrier will be very ill. Only one family of these 7 did not do blood tests for other children.

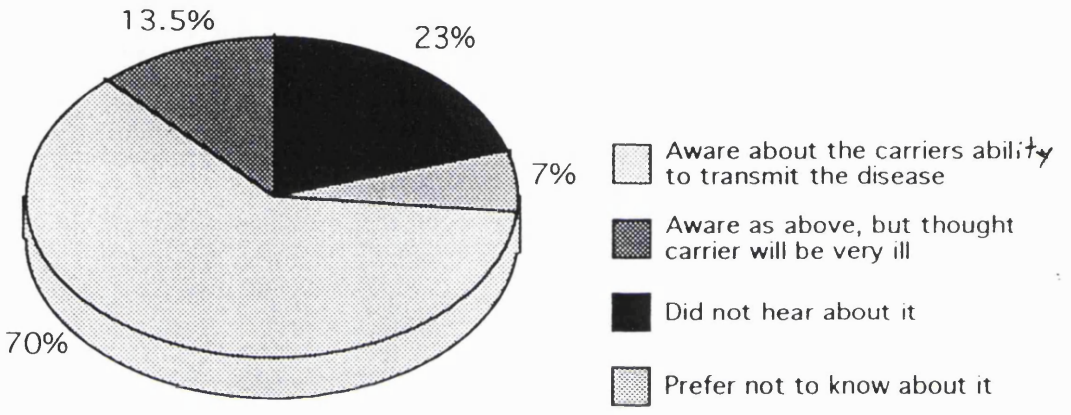
16 (30%) families were not aware of the presence of traits, 12 of whom (75% of sample = 23% of total population) did not hear about it. Such percentage

(75%) has its implications on the quality of genetic counselling and its emphasis.

Only 4 (25% of sample = 7% of total population) prefer not to know about it.

Figure No 4. Knowledge about the carrier state

% is of those who knew it is inherited (47 = 90.4% of total population).



6.2.5. The risk concept

Two questions assess indirectly the parental awareness of the 1 in 4 recurrence risk.

• Their knowledge was rather satisfactory. 35 (67%) knew that some of their children may be affected after they have had the first affected child. While only 9 (17%) were convinced that the fact they already had given birth to an SCD child guaranteed them healthy children afterwards.

• The question of whether this risk persists in each pregnancy was rather difficult. 20 (39%) did not know the answer. While 10 (19%) thought that the risk disappears in subsequent pregnancies once they have had an affected child, which coincides with the parents' response to (Unlikely any will be affected : 17%), 42% knew that the risk persists in each pregnancy.

Table 6 The risk concept

	After they have had the first affected child	Number	%
1	• Some may be affected	35	67
	• Unlikely any will be affected	9	17
	• Likely all will be affected	1	2
	• Do not know	7	14
	The risk of having an affected child		
2	• Persists in each pregnancy	22	42
	• Disappears once they had an affected child	10	19
	• Do not know	20	39

6.2.6. Either sex affected by SCD

Only 14 (27%) families knew that SCD affects both sexes equally. 31 (60%) did not know the answer. There were 7 (13%) families who thought that the disease affects boys more than girls. Index children of 6 of these 7 families were boys, which might be a source of their information.

6.2.7. Risks of cousins' marriages

Families' response to this question was impressive. *48 (92%) were convinced that cousins' marriages imply increased risk of the disease.* Considering the relatively high ratio of: consanguinity/1st cousins: 61.6/30.8% amongst the population sample, the response reflects good awareness. Four families thought that cousins marriages are not responsible about this increased risk. Marriages of two of whom were consanguineous.

6.2.8. Screening before marriage

Almost all studied families - *50 (96%) - wanted to screen couples who contemplate marriage.* Many of them expressed their desire for an obligatory

lawful screening to be performed before documenting marriages. They chose this option as a method of reducing the occurrence of SCD in their country.

Bearing in mind that 38.4% of studied parents are non-consanguineous, families' demand was to screen all couples before marriage, regardless of a previously documented SCD in their families.

Considering the habit of arranged marriages between families in this society, some of the studied parents suggested that both families of the proposed bride and groom should be asked to disclose to each other about the presence of the disease in their families, particularly about the proposed couple's carrier status.

Parents took an opportunity of this question to tell about tragedies of divorces occurring after giving birth to affected children, because families, although aware of it, did not tell one another about their carrier daughter/son before marriage. Other parents were so enthusiastic and asked the investigator to promise that *their desire for an obligatory screening before marriage would be brought up to the Health Authorities.*

6.2.9. Information transfer about SCD inheritance

a) Professional source :

40 (77%) of the population sample were informed by a paediatrician, 10 (19%) by a haematologist, 2(4%) by others and *none by a geneticist.*

Considerable attention was paid to the presence of both parents (83%) when the disease was explained. Only in a minority (17%) of families, the information about the disease given in the presence of one parent.

• The Patients' Diagnostic / Follow up **cards:**

Although 33 (63.5%) families held a Haemoglobinopathy card, given by the haematology unit, and 14 (27%) had a usual hospital card, none of those cards was a source of usable data. The written information was uncompleted, unexplained to parents, and in many instances parents faced a linguistic barrier because English was used in writing these cards.

b) Sources of extra information:

28 (54%) of the respondents sought information from other sources. Among whom 12 (43%) of sample were able to travel abroad, reflecting the habit and the accessibility of seeking medical help abroad, which people in this society can afford. The mass media (T.V. , newspapers, or reading a leaflet), contributed only to 50% of choices (27% of respondents) as in table 7.

Table 7 Sources of extra information

Source	Number	% of sample	% of population sample
Travel abroad	12	43	23
Leaflets and brochures	7	25	13.5
Parents who had a similar child	11	39	21
Media (T.V. and Newspaper)	7	25	13.5

c) Transmission of information in the family about affected/carrier members.

The index studied child was the first affected in the family in 39 (75%) of population sample.

Although the birth of an SCD child implies an increased risk for other relatives of being carriers of the SCD gene, the hereditary aspect of the disease is not often discussed with these relatives, particularly with proposed couples or parents in their reproductive life.

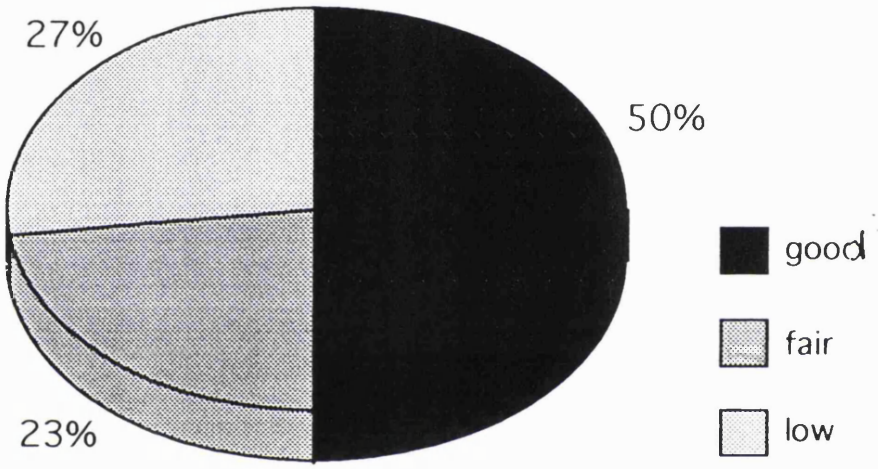
24 (46%) of families knew about a relative affected, 12 of whom (23% of population) knew about it before they had planned for the affected child. Only in 5 (10% of population) was information transmitted from a relative about the

possible risk of giving birth to an affected child, before they had planned to produce the affected child.

6.2.10 Knowledge score distribution

Figure No 5

Parents' knowledge about genetic transmission of SCD



26 (50%) families scored "good" knowledge, 12 (23%) scored "fair", and 14 (27%) scored "low" knowledge. Affected families are expected to have detailed knowledge and higher scores. More than 80% - > 90% of parents in another autsomal recessive disease, scored correct answers on genetic transmission of the disease.[77] In community studies conducted elsewhere, general population scored lower knowledge about a similarly inherited disease.[70]

Table 8 Index of overall knowledge (N = 52)

No	Grade	Good		Fair		Low	
		N	%	N	%	N	%
1.	Parents interviewed Mother N = 26 Fathers N = 8 Couples N = 18	 12 5 9	 46 62 50	 6 3 3	 23 38 17	 8 0 6	 31 0 33
2	**Education** **Fathers (Fathers + Couples) N = 26** College+ N = 9 High School N = 4 Primary School N = 12 None N = 1	 6 0 8 0	 67 0 67 0	 1 3 1 1	 11 75 8 100	 2 1 3 0	 22 25 25 0
	Total	**14**	**54**	**6**	**23**	**6**	**23**
	Mothers N = 26 College N = 6 High School N = 3 Primary School N = 11 None N = 6	 5 2 5 0	 83 67 46 0	 0 0 3 3	 0 0 28 50	 1 1 3 3	 17 33 28 50
	Total	**12**	**46**	**6**	**23**	**8**	**31**
3	**Income** (Thousand KD/year ***20 - 35 (N = 4)*** 10 - 20 (N + 28) 3 - 10 (N= 15) < 3.5 (N = 5	 ***4*** 16 4 2	 ***100*** 57 27 40	 ***0*** 5 6 1	 ***0*** 18 40 20	 ***0*** 7 5 2	 ***0*** 25 33 40
4	**Professional Information** ***By a Paediatrician (N = 39)*** By a Haematologist + others (N= 13)	 ***20*** 6	 ***51*** 46	 ***9*** 3	 ***23*** 23	 ***10*** 4	 ***26*** 31
5	**Extra Information** Sought for (N = 28) Did not seek for (N = 24)	 15 11	 54 46	 5 7	 18 29	 8 6	 28 25
6	**Age groups** (parents) 24 - 33 (N = 19) ***34 - 40 (N = 30)*** 41 - 50+ (N = 21)	 9 ***16*** 10	 47 ***54*** 48	 4 ***7*** 4	 21 ***23*** 19	 6 ***7*** 7	 32 ***23*** 33

• **Analysis of index of overall knowledge**

Conclusions here are not solid because of the small numbers. As shown in the table 8 parents scored more "good" knowledge when they were interviewed as fathers (62%) and couples (50%) than as mothers alone (46%).

- Analysing knowledge according to parents' education:

Fathers' education was taken into consideration when the interviewees were couples, which produces fathers and couples sample of (26), for comparison with mothers' education (N = 26).

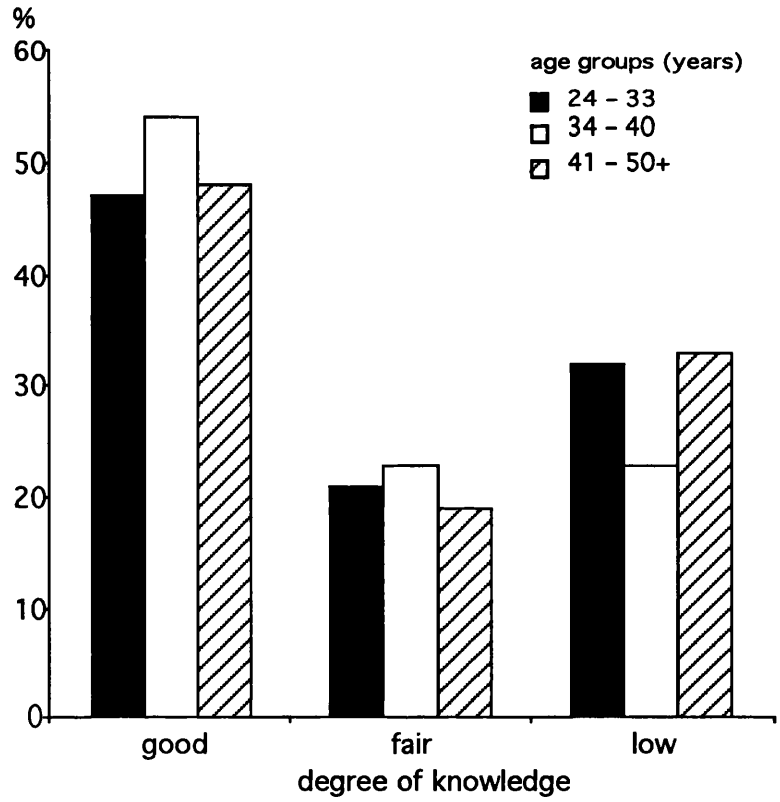
- Fathers and couples scored more "good" knowledge (54%) than mothers (46%) and less "law" knowledge (23%) than mother (31%). Fathers and mothers were equal at "fair" knowledge (23%).

- Parents who had higher incomes scored more "good" and less "low" knowledge than those of lower incomes who scored more "fair" and "low" knowledge.

-Parents who were informed about the disease by paediatricians scored more "good" and less "low" knowledge than those who were informed by haematologists and other health professionals.

- Families who sought extra information scored more "good" knowledge than those who did not, but at the same time the former scored less "fair" and more "low" knowledge than the latter. Which is not conclusive.

Figure No 6 Comparison of degree of knowledge between the 3 age groups of families.



Middle age group parents (34-40) scored more "good" and less "low" knowledge than the younger (24-33) and the older (41-50+) age groups.

6.3. Parents' behaviour after diagnosis of SCD child

6.3.1 Children produced by studied families and their blood tests

The 52 families gave birth to 261 children, with a mean of 5 (SD : 2.1), among whom 144 (55.2%) were identified as inheriting Hb.S, with a mean of 2.7 (SD : 2.3). 82 (57%) were homozygous. Numbers of identified SCD children are underestimated, because 14% of families did not do blood tests on their other children after diagnosis of an affected child. And because 85% of families did blood tests on their children, but they screened some and not all of their children. It was obvious that families responded only once when they were advised to screen for SCD. They were not enthusiastic about screening children whom they produced later, or who could not attend the first screening session.

Table 9: Comparison of knowledge score between those who did blood tests on their other children and those who did not do so.

Knowledge score	Good		Fair		Low	
	N	%	N	%	N	%
Did blood tests (N = 44)	22	50	11	25	11	25
Did not do blood tests (N = 7)	4	57	0	0	3	43

The numbers are small to draw a conclusion. However, 4 families although they scored high knowledge, were among those who did not do blood tests on their other children.

Blood tests and awareness of the presence of carriers:

Although 44 (85%) families did blood tests on their other children after diagnosis of their affected child, only 36 (81.8% = 69% of population) were aware that some of their children can pass on the disease to their offsprings.

6.3.2. Behaviour towards delaying further pregnancies after diagnosis of the affected child.

a) Families who wanted to delay further pregnancies:

28 (54%) families attempted to delay further pregnancies. A substantial number, 21 (75%) of them could actually delay, among whom 15 (72%) used contraceptive pills for this purpose. The remained 7 families produced unplanned children.

Table 10

Behaviour of those who wanted to delay further pregnancies:

N = 28 (54%)

Behaviour	Number	% of sample	% of total population
Wanted to delay	28	100	54
Could actually delay	21	75	40
Method used to delay (N = 21)			
Pills	15	71.4	28
I.U.D.	3	14.3	6
Safe period	3	14.3	6

• The reasons why 24 (46%) families did not want to delay further pregnancies are shown in table 11.

Acceptance of Faith was a reason in only 10 families (19%), which reflects a modification of the deeply rooted beliefs in this society. Lack of mutual agreement between partners was a reason in only 4 (8%) families. However, 15 (29%) were hopeful for another healthy child.

Table 11

Reasons why 24 (46%) families did not want to delay further pregnancies

Reasons	* Number	% of sample N = 24	% of total population N = 52
Hopeful for another healthy child	15	44	29
No mutual agreement with partners	4	12	8
Accepted faith	10	29.3	19
Had enough children	5	14.7	10

* Numbers of given answers = 34 are not mutually exclusive, because more than one answer was expected.

b) Reproductive behaviour of those who did not delay further pregnancies because they were hopeful for another healthy child N = 15 (29%) families:

Birth rank of first affected child amongst these families ranged between 1 and 5 (mean - 1, SD - 1.2). Their number of pregnancies until diagnosis ranged between 1 and 15 (mean - 4, SD - 3.4), and number of their pregnancies after

diagnosis ranged between 0 and 6 (mean - 2.5, SD - 1.7). This result shows that even though some of these families had > 10 pregnancies, they were still hopeful for another healthy child, to the extent of having 6 pregnancies after diagnosis of an affected child.

c) Comparison of knowledge score and of mothers' education between those who wanted and those who did not want to delay further pregnancies after the affected child was diagnosed (table 12)

Table 12

Knowledge score	Those who wanted to delay N = 28		Those who did not want to delay N =24	
	N	%	N	%
Good	15	**54**	11	**46**
Fair	7	25	5	21
Low	6	21	8	33
Mothers' Education	N	%	N	%
College +	7	**25**	5	**21**
High School	6	**22**	3	**12**
Primary School	11	**39**	10	**42**
None	4	**14**	6	**25**

Figure No 7 Mothers' education in families who wanted and families who did not want to delay further pregnancies.

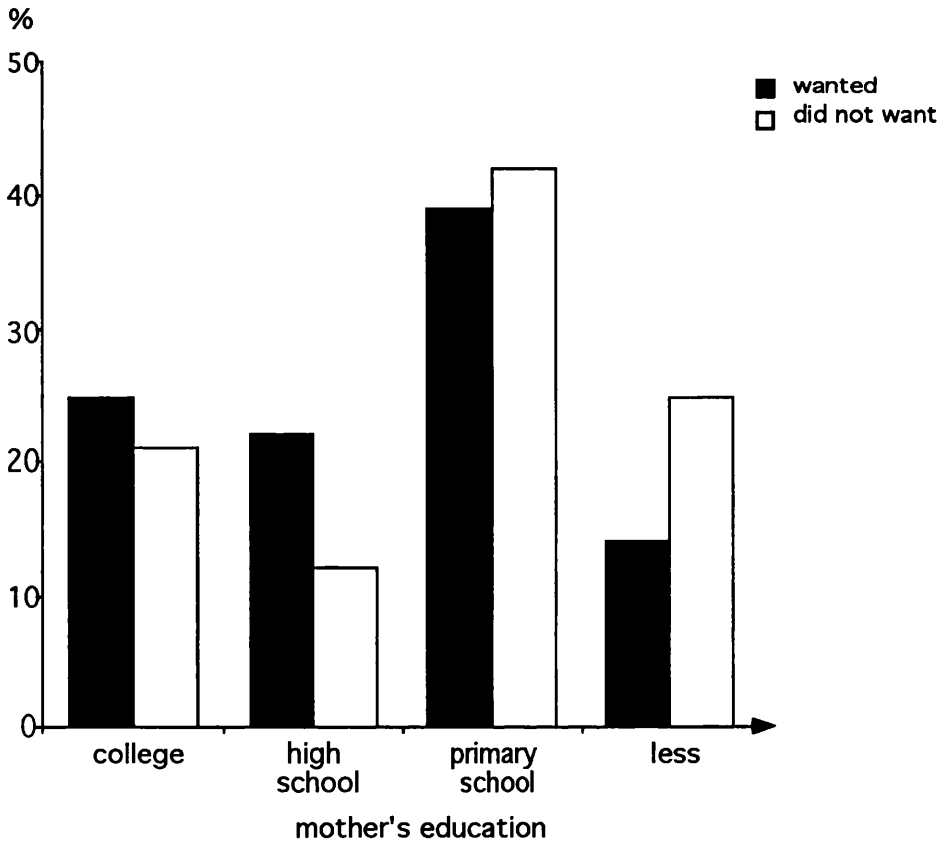


Table 12, and figure 7, show that families who wanted to delay further pregnancies (N = 28) scored more "good" and "fair" and less "low" knowledge than those who did not want to delay further pregnancies (N = 24).

Mothers of families who wanted to delay further pregnancies were more educated. These were the "College" and "High School" graduates, and less "Primary School" and "lower" graduates, than the other group of those who did not want to delay further pregnancies. However, number are small to be conclusive.

6.3.3. Pregnancies occurring in the studied families, before and after diagnosis of the first affected child: N. of families = 52 (table 13)

Table 13

Pregnancies	Number	Mean	SD
Total number of pregnancies	305	5.8	2.6
Number of pregnancies before diagnosis	193	3.7	2.5
Number of pregnancies after diagnosis	112	2	1.8

In general, the above table shows that studied families had less pregnancies after diagnosis of an affected child (mean - 2, SD - 1.8) than they had before diagnosis (mean - 3.7, SD - 2.5).

6.3.4. Birth rank of the first diagnosed child: its influence on family's attitude. Whether they wanted or did not want to delay further pregnancies (table 14).

Table 14

Birth rank of first diagnosed child	1		2		3 - 5		6+	
	N	%	N	%	N	%	N	%
Wanted to delay (N = 28)	14	50	7	25	5	17.8	2	7.2
Did not want to delay (N =24)	6	25	8	33.3	7	29.1	3	12.5

Table 14 shows that when the first diagnosed child was the first born, families who wanted to delay further pregnancies (50%) out numbered those who did not want to (25%). This result is not conclusive, because apart from the small numbers, by the time the first born child was diagnosed other children had already been born in some cases.

6.3.5. Reproductive behaviour of those who do not intend and those who do intend to have more children, at the time of conducting the interview:

35 (67% of the population) families do not intend to have more children, amongst whom 10 (19% of the population) families stopped further pregnancies after diagnosis. While 16 (33%) families intend to have more children.

Analysing the reproductive outcome of two groups: those who stopped further pregnancies, and those who still intend to have more children after diagnosis (Table 15), shows that the first group's decision is influenced by the size of their families: mean number of pregnancies of those who stopped further pregnancies: 7 (SD : 3.8), while it is 4.3 (SD : 2) in those who still want more children.

Mean number of children in the first group is 6.2 (SD : 3) while it is 3.7 (SD : 1.6) in those who intend to have more children.

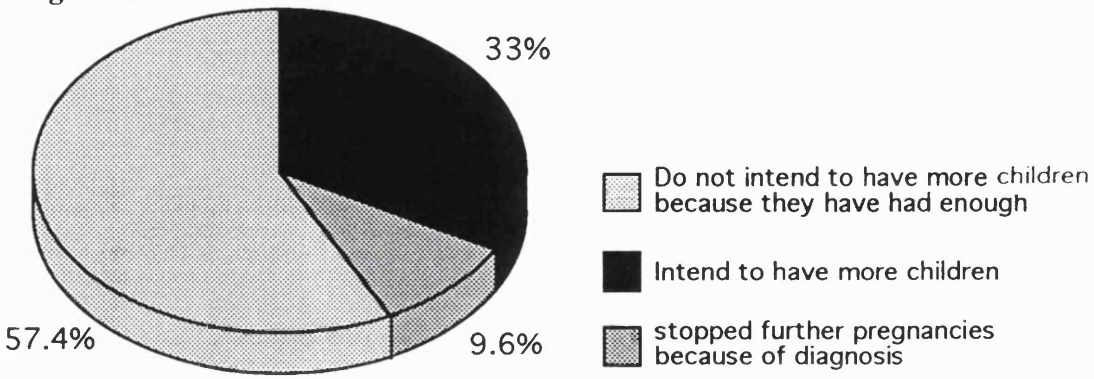
However, only 5 (9.6%) families stopped producing more children because of diagnosis (Table 15). Mean number of children among them was 4.8 (SD : 2.4), which is more than that of those who intend to have more children: 3.7 (SD : 1.6). This points to the influence of family size on decision making.

Table 15 Comparison of reproduction of families at the time of conducting the project.

Reproductive behaviour group	• Total number of pregnances				• Number of children			
	Sum	Range	Mean	SD	Sum	Range	Mean	SD
•Did not produce children after diagnosis (N = 10 19%)	63	1 - 15	7	3.8	49	1 - 8	6.2	3
•Intend to have more children (N = 16 33%)	70	1 - 10	4.3	2	60	1 - 7	3.7	1.6
• Stopped further pregnancies because of diagnosis (N = 5 9.6%)	26	5.2	5.2	2.3	25	2 - 8	4.8	2.4

Table 15 compares reproductive behaviour of those who did not produce children after diagnosis, those who intend to have more children and those who stopped further pregnancies because of diagnosis. Although the numbers are small, the table shows that those who still intend to have more children, had smaller family size (mean N. of pregnancies 4.3 and of children 3.7) than those who did not produce children after diagnosis (mean N. of pregnancies 7 and of children 6.2), and still smaller than those who stopped further pregnancies because of diagnosis (mean N. of pregnancies 5.2 and children 4.8).

Figure 8 Families' reproductive behaviour after diagnosis



6.3.6. Comparison of knowledge score between those who stopped further pregnancies after diagnosis, and those who intend to have more children:

Families who stopped further pregnancies after diagnosis scored more "good" knowledge, and less "low" knowledge than those who intend to have more children, but numbers are small to be conclusive (see table 16).

Table 16

Comparison of knowledge score between those who stopped further pregnancies and those who intend to have more children.

Reproductive behaviour group	Good		Fair		Low	
	N	%	N	%	N	%
Stopped further pregnancies N = 10	6	60	1	10	3	30
Intend to have more N = 16	7	44	4	25	5	31

Table 17

6.3.7. Comparison between characteristics of families who do intend, and who do not intend to have more children.

1	**Knowledge:**	**Good**		**Fair**		**Low**	
		N	%	N	%	N	%
	Intend (N = 16)	7	44	4	25	5	31
	Do not intend (N = 35)	18	51.5	8	23	9	25.5
2	**Children number:**	**Sum**		**Range**		**Mean**	**SD**
	Intend (N = 16)	60		1 - 7		3.7	1.6
	Do not intend (N = 35)	197		2 - 10		5.6	2
3	**Education (mothers):**	**College+**		**High School**		**Primary School**	**Less**
		N	%	N	%	N	%	N	%
	Intend (N = 16)	5	31	4	25	6	38	1	6
	Do not intend (N = 35)	6	17	5	14	15	43	9	26
4.	**Income (thousand KD / year**	**20 - 35**		**10 - 20**		**3.5 - 10**	**< 3.5**
		N	%	N	%	N	%	N	%
	Intend (N = 16)	0	0	9	56	5	31	2	13
	Do not intend (N = 35)	3	9	19	54	10	28	3	9

The analysis clearly shows the small numbers. However, it shows that families were not influenced by their socio-economic or knowledge standards, but by the numbers of chilren they have had.

Social Outcome of the study

6.3.8. Impact of the presence of affected children on marriages

Questions 50 and 54 *stimulated parents to speak about social tragedies*, as broken marriages.

Question 50 enquired into possible disclosure between proposed partners about carrying the trait. Question 54 collected families' views on screening before marriage.

- A 50 year old mother (family no.49) knew that members of her family carried the trait. With bitterness and anger she spoke about divorces between couples, and conflicts between families, after diagnosis of affected children. Families blamed one another for not disclosing their son's/daughter's carrier status before marriage.
- Another example was given by family no.13, whose parents responded readily and appeared immediately at the interview. One of their relatives knew that she was a carrier of SCD. *She explained to her fiancé who refused to be screened for the disease before marriage.* She obtained a divorce after having had 3 affected children. She refused to re-marry and was devoted to her ill children. This shows deficient awareness.

• Broken marriages in studied families

1. Family no. 4 : 31 year old mother was married to a far cousin, who divorced her after diagnosis of their 4th born child. The second marriage was not consanguineous. Birth interval between the affected child of her first marriage, and the apparently healthy child of her second marriage, was 7 years. She thought that the cause of SCD is unknown. This is again a deficient awareness.

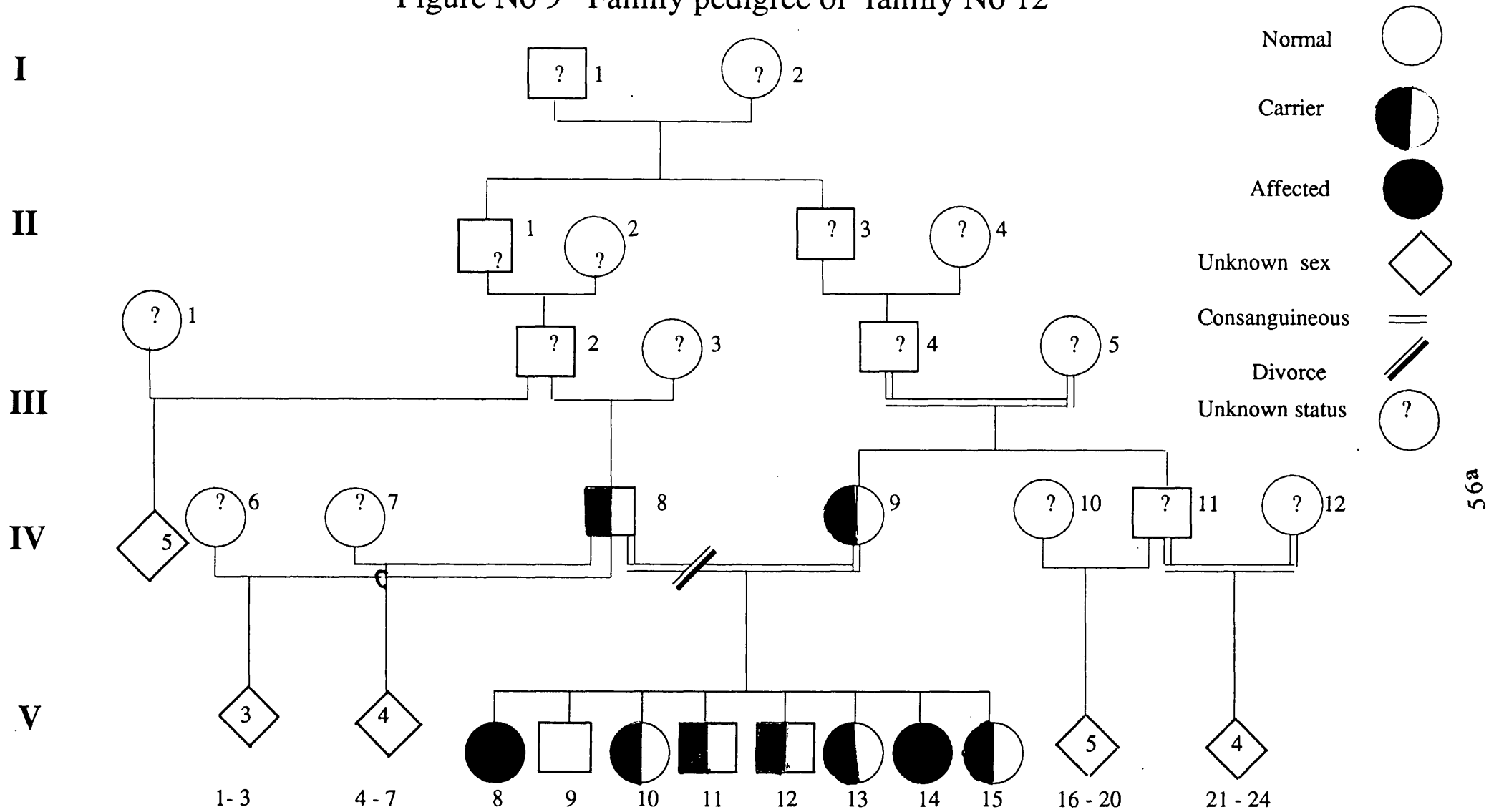
2. Family no 12 : 40 year old mother. The outcome of her consanguineous marriage was : one healthy, two affected and five carrier children. Her husband divorced her. His 7 children of second and third marriages were apparently healthy, (their definite status was unknown) which gave him a reason to blame his first wife for transmitting the disease to their children, and to claim that he was free from the disease. This mother and her brother were the result of a consanguineous marriage. Her brother produced 9 children of two marriages, one of whom was consanguineous, unaware of the possibility of him transmitting the disease to his own children. The tragedy of his sister did not stimulate him to screen his children, and he was not informed.

This interviewed mother was socially and psychologically insulted. Her feelings of guilt were enormous. She struggled unassisted for the life of her affected and carrier children. Several attempts were made to meet the father but did not succeed.

Figure 9 shows the family pedigree (page no 56 a)

3. Family no. 51: 48 year old father. The outcome of his first (first cousin) marriage was one affected and 3 carrier children, because of whom he divorced his wife. She remarried. He did not know about her further produced children. His second marriage was not consanguineous. The outcome was "3 symptomatic carrier children", as he said. He blamed doctors and said: *"They always asked: Is your wife a relative? So I divorced her."* He probably got other SCD children from his second marriage and he did not understand the carrier status.

Figure No 9 Family pedigree of family No 12



6.4. Attitudes of studied parents

6.4.1. Attitudes towards information transfer about the genetic transmission of SCD to offsprings

Parents who were aware of the presence of carriers among their own children (N = 36) were asked whether they intend to explain to their children who carry the trait about the disease. *All families (36) showed positive attitude to this question.* And all of them intended to explain about the disease to both sexes. 72% of these families scored "good" and 22% scored "fair" knowledge.

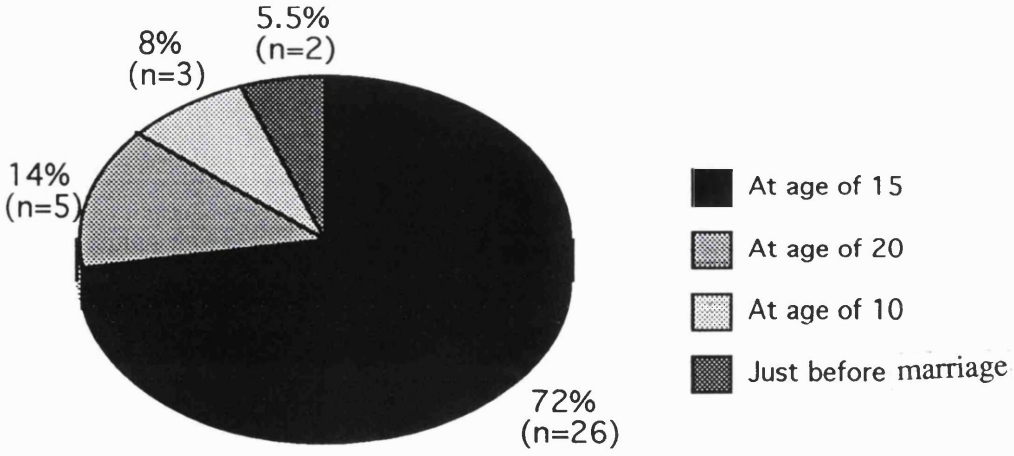
The 16 families who were not aware of the presence of carries among their children, scored "fair" (75%) and "low" (25%) knowledge.

The best age of information transfer about the disease transmission.

The 36 families who were aware of the presence of trait carriers in their children were asked at what age it would be best to explain to their children about it.

Most parents (N 26, = 72% of sample) plan to give their children information on the subject at the age of 15 years. Only 2 families plan to do this just before marriage (Figure No 10).

Figure No 10 The best age for information transfer.



6.4.2. Attitudes towards disclosure about the disease between partners.

Families who were aware of the presence of the trait among their children (N = 36) were asked whether they would advise their carrier daughter/son to tell her/his partner about it before marriage. *All but one had a positive response.* The negative responder was a father who divorced his first cousin wife, after having had affected children, and produced affected children too from his second non-consanguineous marriage. This unawareness has its implications on the urgent need for genetic counselling.

- **Attitudes towards screening**

Families' views were sought on screening in the first week of life, and on foetal diagnosis in the first few weeks of pregnancy.

6.4.3. Neonatal screening

50 (96%) families wanted to screen for the disease and the trait carrier in the first week of life. They appreciated the test and wanted it to be legally performed on every newborn.

Parents' comments in their own words:

- *"I want it in order to prepare for the child's care".*
- *"Yes, this would offer early medical help and better care".*
- *"It will help me to make proper plans".*
- *A father who knew the diagnosis after the 6th born child, 4 of his children were affected, and 2 carried the trait:*

"If it were done, my wife and I could have better plans. Because of late diagnosis my children suffered, and our life became miserable".

- A mother who was divorced by her consanguineous husband after the 8th born child, 2 of her children were affected and 5 carried the trait:

"The disease has ruined my life. Why do we have to sacrifice ourselves so long before diagnosis?"

2 families refused neonatal screening. Each had only one affected child, and a family size of 3. They thought that the test is not useful because there is no actual treatment.

- *"No use of this test. If the disease is there, it will remain".*
- *"It is inherited and it will persist".*

6.4.4. Prenatal diagnosis.

38 (73%) families agreed on the foetal diagnosis during the first few weeks of pregnancy, if the test were available in Kuwait.

These were:

18 mothers = 69.2% of interviewed mothers.

7 fathers = 87.5% of interviewed fathers.

13 couples = 72.2% of interviewed couples.

It is surprising that these parents hardly questioned the test safety and technique. One father of those who rejected the test was too concerned about mother's safety. One couple commented that the test would induce anxiety.

Table 18

Comparison of knowledge score, mothers' education and income between those who accepted prenatal diagnosis and those who did not accept.

1. Knowledge score	Good		Fair		Low	
	N	%	N	%	N	%
Accepted (N = 38)	19	50	10	26	9	24
Did not accept (N =14)	7	50	3	21	4	29

2. Education	Accepted (N =38)		Did not accept (N = 14)	
	N	%	N	%
College	7	19	5	35.5
High School	6	16	3	21.5
Primary School	18	47	3	21.5
Less	7	18	3	21.5

3. Income thousand KD/ year	Accepted N = 38		Did not accepted	
	N	%	N	%
20 - 35	3	8	1	7
10 - 20	19	50	9	64
3.5 - 10	11	29	4	29
< 3.5	5	13	0	0

The numbers in the table 18 are small to make any conclusion about the influence of knowledge, education and income, on families' decision to prenatal diagnosis.

6.4.5. Termination of pregnancy, if the prenatal diagnosis test were positive:

38 families who would accept the prenatal diagnosis test were asked if they would carry on with pregnancy, in case the test were positive.

Only 12 (31.5%) families wanted to terminate such pregnancy = 23% of total population sample.

They were 5 mothers, 6 couples, and 1 father.

24 families (63.2%) = 46% of total population sample wanted to carry on with pregnancy.

2 families (5.3%) = 4% of total population sample were uncertain.

They were hesitant and worried about mother's health if termination were done. One of whom was a father who had 2 children, and the other were a young couple who had only one child. Both families intended to have more children.

It was uncomfortable to learn later that an interviewed mother was pregnant at that time of questioning the issue of possible termination.

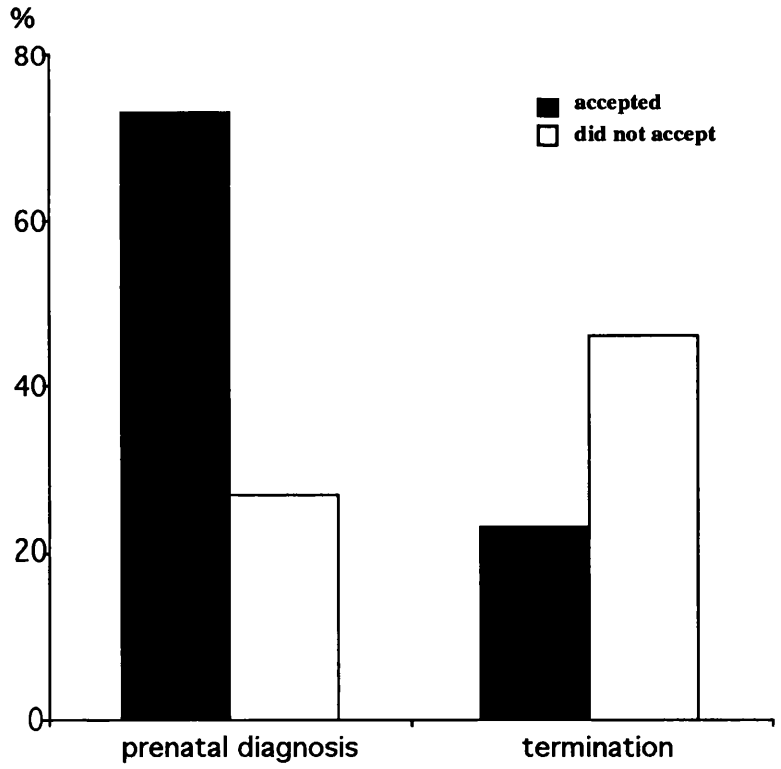
Table 19 Prenatal diagnosis and termination acceptance

Attitude	Prenatal diagnosis (N = 52)		Termination of an affected foetus (N = 38)		% of total (N=52)
	N	%	N	%	
Accepted	38	73	12	31.5	23
Did not accept	14	27	24	63.2	46
Uncertain	0	0	2	5.3	4

The question about termination of pregnancy was the last of the long questionnaire. Addressing termination of pregnancy, in such a conservative Muslem society was not without possible serious reactions. The question seemed to be a surprise for many parents. Their faces turned red, their eyes rolled up, they gazed at me, they thought, then answered peacefully. *It was obvious that this was the first time to be questioned about and to think of termination of an affected foetus.*

Figure No 11

Acceptance of prenatal diagnosis and of termination of affected foetuses.



This question would initiate serious arguments if it were asked to general population rather than to affected families.

6.4.6. Characteristics of families who "accepted" termination of pregnancy and those who "did not accept" it or were uncertain (see table 20).

Table 20

Knowledge score	Good		Fair		Low	
	N	%	N	%	N	%
Accepted (N = 12)	7	58.3	3	25	2	16.7
Did not accept (N = 26)	12	46.2	6	23	8	30.8

Education	College		High School		Primary School		None	
	N	%	N	%	N	%	N	%
Accepted (N = 12)	5	41.6	1	8.4	5	41.6	1	8.4
Did not accept (N = 26)	5	19.2	3	11.6	13	50	5	19.2

Income In thousand KD per year	20 - 35		10 - 20		3.5 - 10		< 3.5	
	N	%	N	%	N	%	N	%
Accepted (N = 12)	2	17	7	58	1	8	2	17
Did not accept (N = 26)	1	3.8	12	46.2	10	38.5	3	11.5

Analysing characteristics of families who "accepted" termination if the prenatal test were positive revealed the following:

1. Knowledge: these families were more knowledgeable about the disease than those who did not accept or were uncertain.Families who

accepted termination scored more "good" and "fair" knowledge and less "low" knowledge than those who did not accept.

2. Standard of education: education of the parent by whom the interview was given is calculated. In case of a couple, father's education is taken.

Families who "accepted" termination have higher percentage of highly educated and less percentage of lower educated parents than those who did not accept or were uncertain.

3. Income: Percentage of families with high income (20-35 and 10-20 thousand KD/year) were more among those who "accepted" than among those who did not accept or were uncertain. Taking the small numbers into account, families who would accept termination of an affected foetus were influenced by their knowledge about the disease and their socio-economic standards.

7 Discussions

7.1. General discussion

Although no comprehensive surveys have been done in Kuwait, it is known that sickling disorders are common in the region bordering the western coast of the Arabian Gulf.[3,11,15]

The description of the milder form of SCD in the Eastern province of Saudi Arabia,[21,76] has been also noted in Kuwait.[4,10] Thus it is probably peculiar to Arabs of this region with a common ancestry among those from Kuwait and Saudi Arabia. Awareness of the gene frequency in Saudi Arabia,[3] has stimulated further scientific depth into SCD there.[7,16,20,23] Whereas this is not the case in Kuwait.

• The fact that SCD patients were not under regular follow-up, and their contact with the haematology unit was not maintained, made it such a difficult task to collect them, 34 families dropped from the original sample size because of lack of updating their addresses. However this acted positively in the reachable families' prompt response to the interview. Their desire to talk and to discuss issues related to the influence of SCD on their lives was obvious.

• Mothers outnumbered fathers in the total sample by 1.6 : 1, almost half (51.4%) of the families responded as couples. This might reflect more interest among mothers, but might also be influenced by the fact the investigator was a female, and that all interviews were in the hospital.

• The outcome of this study could have been more relevant if only parents in their reproductive age were interviewed. Because of the limitations of the sample size, the eldest parent was 55 years and the youngest 24. This point could be considered in further studies about SCD in Kuwait.

7.2. Impact of SCD on patient

It was not in the project design to study clinical impact of the disease. But it seemed logical to start by asking about data related to the index child himself. 78.8% of the patients were < 15 year of age.

7.2.a. Length of time before diagnosis:

It shows clearly the importance of early diagnosis and the deficient awareness. Nearly half (48%) of patients suffered before diagnosis. Length of time ranged between one month and 9 years. Families positive response to neonatal screening is therefore not surprising. If early diagnosis were made, patients would suffer less, and their parents would at least space their pregnancies or choose another plan for their family.

7.2.b. Admission to hospital

43(82%) of studied patients were admitted to hospital. The fact that 6(13%) of homozygous patients were not admitted, (compared to (8%) in Brent, UK[26]) and 3(50%) of heterozygous were admitted, shows the variability of the disease, and coincides with others' observations about SCD in the Arabian Peninsula.[7,11,76] Further studies of the interactions with SCD in the patients in Kuwait is required. The decision to admit is subjective and may not necessarily reflect the increased severity of vaso-occlusion. In a study from Saudi Arabia,[23] a severity index was used and found that patients from Al-Qatif had the lowest severity index, and those from Jeddah, Mecca, Taif and Medina the highest.[23]

7.2.c. Death rate

From causes related to SCD was 13.5%, compared to: 10% in Saudi Arabia in under 15 year of age,[15] 10% in Jamaica in the first year of life and 3% in the third,[76] and 10% in Los Angeles during the first decade of life.[78] It was not among the objectives of this study to identify age at death in SCD patients, and the numbers are small to do so. In the affluent society of Kuwait, living standards and the ready access to medical care, would presumably play a part in improving patients' conditions, and in reducing death rate, if they were associated by increased awareness of the disease manifestations among affected families.

7.3. Knowledge

Affected families having had experienced the disease manifestations and complications are expected to score a high knowledge about it. The 50% "Good" knowledge and 23% "Low" knowledge seem rather unsatisfactory, but not bad if it is considered that these families were not subjected to any genetic programme. Would an estimation of the standard of knowledge about SCD in the community be lower? It would be useful to know the answer.

7.3.1. Understanding the aetiology

Almost all 47(90.4%) knew that it is and inherited disease. But only 59% of these (i.e. of total) knew that it is transmitted from both parents, whereas 97% of parents of cystic fibrosis understood this concept.[77] Some parents (10% of total) thought that it is transmitted only from either parent. This explains why in some cases parents blamed one another for having an affected child and ultimately social conflicts occurred. The concept of "inheritance" was not well absorbed in their minds, for some of them did not know that if a maternal cousin was affected, their own children could be at risk. Although their

responses showed understanding the recessive transmission, the terminology "recessive" was not used in the questionnaire, but it was mentioned and explained to them in the intervention session which followed the questionnaire. Parents have the right to be well informed, time and patience have to be devoted as well as readiness to listen and to answer.

7.3.2 Understanding the carrier state

It is necessary and the right of each affected family to be aware of the presence of carriers, who is the carrier among their children and what does being a carrier mean? Otherwise, how do we expect them to plan for a healthy future by having children free from SCD? Although 70% of families were aware of the presence of a carrier and of the risk of him/her transmitting the disease to his/her children, yet 30% were not aware. Having 12 (23%) families in this small sample sized study not hearing at all about a carrier is a clear sign of how essential a well informed counselling is. The consequences of carrier-carrier mating and a carrier-non-carrier mating were explained to them after the interview. Whereas these consequences were well understood by parents of cystic fibrosis patients in a similar study by 97% for the former consequence and by 84% for the latter.[77]

7.3.3 The risk concept:

Although 67% of parents knew that some of their children may be affected after they have had the first affected child, only 42% realised that they have the "same" risk in "all" subsequent pregnancies. Parents' response in similarly inherited diseases is variable. 50% knew this is a risk they have at each subsequent pregnancy, whereas in another 86% of respondents knew the risk persists in any pregnancy.[77] Studied parents recalled that their doctors did mention the 1 in 4 or the 25% and 50%, but they were confused about it.

Genetic counselling could be effective if it could be repeated in subsequent follow-up visits.

7.3.4. Informing the carrier child about it, and when to do so:

All parents who were aware of the presence of a trait carrier amongst their children wanted to transfer information about the transmission of the disease to their children. Most parents (72%) elected *the age of 15 years* to explain to their children about it. Such positive response has to be supported by maintaining good contact with these families, counselling them on their queries, and perhaps by distributing simplified leaflets to carriers around the age of 15, or inviting them to a session of video or conversation with the counsellors, and providing appropriate support to youths and their families, so as to have this response translated into reality.

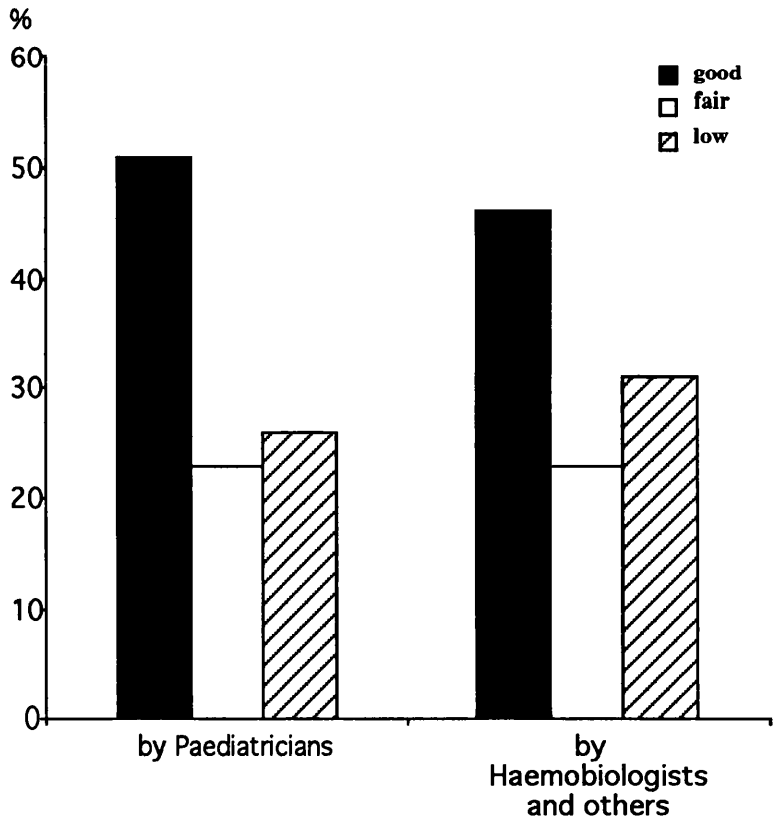
7.3.5 Sources of information

It is obvious that all parents had a professional source of information. Mostly (77%) by a paediatrician. But only half of them (54%) sought extra information.

Although numbers are small, figure 12 shows that parents who were informed by paediatricians were more knowledgeable than those informed by others. It is a misconception that doctors do not have the time to provide genetic counselling, especially in Kuwait with its high doctor/patient ratio (1/570).[79] SCD families' contact with paediatricians is clearly more than with other professions. Training of paediatric counsellors seems an appropriate first step towards developing the necessary service. A team of well trained counsellors

has many advantages.[66] They can encourage more professional interest and research into SCD, they can involve the community in developing a positive attitude towards SCD and in implementing strategies appropriate to the society in Kuwait.

Figure 12 Comparison of degree of knowledge between families who were informed by Paediatricians and those who were informed by Haematologists and others.



The mass media is a well known source of distributing information, especially in Kuwait where people are regular readers of newspapers and watch TV frequently. It proved to be a good channel for sensitization and education of the population in genetic programmes.[63] Only a small group of patients (13.5%) had an access to a leaflet or a TV programme about SCD.

7.3.6. Knowledge influenced by:

7.3.6.a. Interviewees being mothers alone

Figure 13 Comparison of degree of knowledge between two groups: Fathers and couples, and mothers

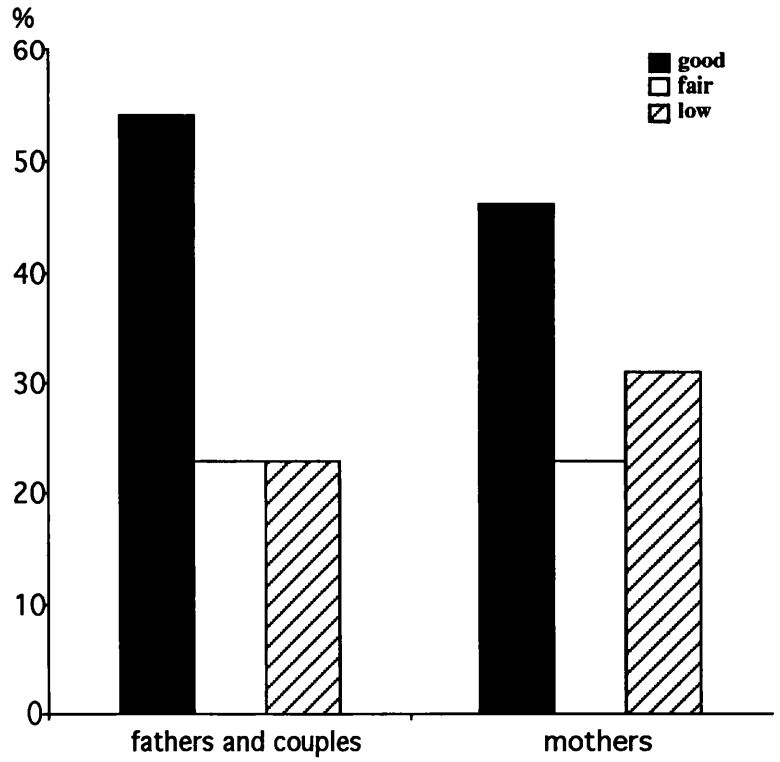


Figure 13 shows that fathers and couples scored more "good" knowledge (54%) than mothers (46%), and less "low" knowledge (23%) than mothers (31%). whereas in a community study about cystic fibrosis, the female score was the better.[70] More attention is required to improve mothers' knowledge about SCD transmission. They are the care providers in the family, and they make and influence family decisions.

7.3.6.b. Income

Figure 14 Comparison of degree of knowledge between the 4 income groups of families

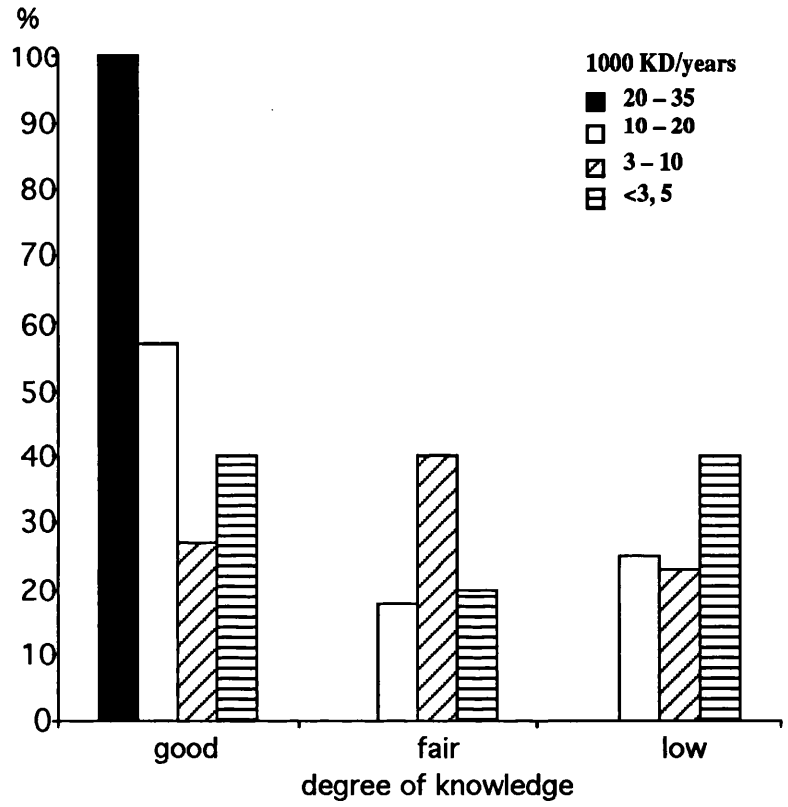


Figure 14 shows that parents who had higher incomes scored more "good" and less "low" knowledge than those of lower incomes who scored more "fair" and "low" knowledge. This is probably because raised incomes would facilitate access to channels of information and knowledge.

7.3.6.c Age group:

Although numbers are small, figure 6 (page 44) shows that the middle age group (34-40 years) were more knowledgeable than others. Probably because they have had more experience with their SCD children and more access to information than the younger age group (24-33 years) who require a well informed decision at their stage of family formation.

7.4. Reproductive behaviour of studied families:

Although the numbers are small, the idea was to determine whether the presence of an affected child in the family had influenced parents' reproductive behaviour and whether their behaviour was influenced by their knowledge about the disease and/or by other factors.

Delaying or spacing pregnancies enables parents to provide care and time for their affected child, and gives them chance for a better planning of their family.

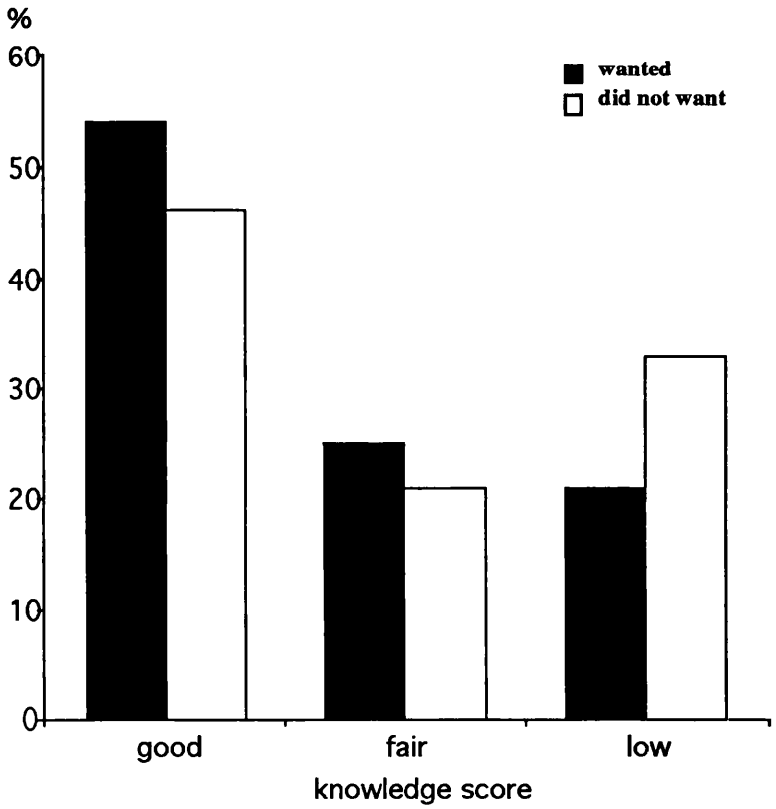
Less than half, 21 (40%) families spaced their pregnancies, and in the absence of genetic counselling *only 5 (9.6%) stopped having more children because of diagnosis of SCD child.* Whereas in spite of diagnosis, 16 (33%) intended to have more children at the time of conducting the project.

Mean number of pregnancies produced before diagnosis was 3.7 (SD 2.5). After diagnosis families produced less pregnancies with a mean of 2 (SD 1.8).

However, at the time of the interview, the reason why 57.4% of families did not intend to have more children was that they have had completed families.

7.4.0. Families behaviour was mainly influenced by

Figure 15 Knowledge of parents who wanted and parents who didn't want to delay further pregnancies after diagnosis of the affected child.



7.4.1. Knowledge

Figure 15 shows that parents who "wanted to delay further pregnancies" after diagnosis of the first affected child, scored higher knowledge than those who did not want to.

Table 17 shows that families who "do not intend" to have more children scored more "good" and less "low" knowledge than those who "intend" to have. This

shows how essential increased awareness is. If the affected families were well informed, they would probably change their reproductive behaviour.

7.4.2. Mothers' education

Furthermore mothers "who wanted to delay further pregnancies" were higher educated than those who "did not want to delay".

Well educated mothers are able to recognise better choices for planning their families. The community in Kuwait has been aware of the females education, and classes for adult women education have been established. However increase community awareness of the roles of women in planning for their families in necessary.

7.4.3. Faith and hope

The fact that only 10 (19%) parents relied upon "faith" in opting not to delay their pregnancies, shows the modification of thinking in that society tempered by education and modernisation. The fact that 15(29% of total) families were hopeful for another healthy child, coincides with others observations that many prospective parents choose to take the chance that their child may not be very severely affected, even though they were well informed.[25] What would be the decision of those 15 families if they were informed in a genetic counselling? the answer will probably be in the foreseeable future.

7.4.4. Family size

Characteristic of parents "who intend to have more children" at the time of conducting the project, and those "who do not intend" to (Table 17), show that mothers who "intend" were more well educated and had less income than mothers who "do not intend". But at the same time, mothers who "intend" had smaller family size (mean number of children 3.7, SD 1.6), than mothers who "do not intend" (mean number of children 5.6, SD 2). Taking into account that

the average family size of Kuwaitis in 1985 was 8.6,[79] decision making of reproduction was influenced by family size they already have had.

7.4.5. Population policies in Kuwait

a) Fertility encouragement

Fertility reduction is the best, and the most widely used way to reduce population growth in the world today. In Kuwait, as part of the five year plan 1985-86 - 1989-90, policies relating to fertility and mortality were designed to maximize the growth rate of Kuwait nationals in order to augment their numbers in the population and labour force,[79] (see appendix 2 about Kuwait). The eventual objective was to achieve a balance between the nationals and expatriates, and ensure that the nationals comprise half the population by 2000.[79] continued high fertility has been encouraged through early marriage and various programmes to reduce the level of infertility. The plan proposed housing patterns suitable for large families.[79] SCD families having had not been well informed, will definitely be influenced by this policy.

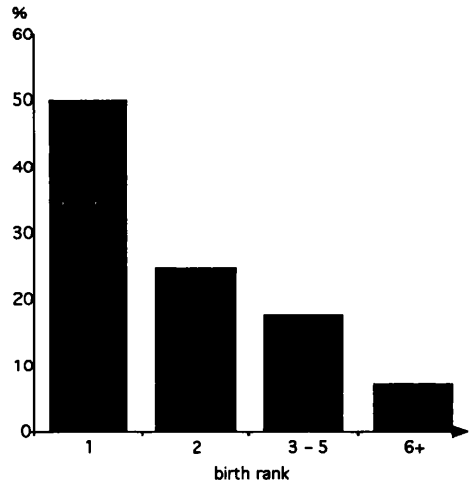
b). The use of contraception

21 mothers (40% of total sample) could actually delay further pregnancies by using contraceptive measures. Compared to (41%) in Kuwaiti national women.[81] The majority 15 (71.4% of the sample) of those who chose contraception, relied on the pill, compared to 85% of such women in Kuwait.[81] Only 3 (14.3%) reported the use of I.U.D., and the same number the traditional method (the safe period) compared to 4% and 6% respectively among such women in Kuwait.[81] Spacing, rather than desire to limit family size, appears to be the motivation for contraceptive use in Kuwait and therefore amongst studied families. Families at risk of thalassaemia major did change their reproductive behaviour when antenatal diagnosis was introduced to them.[66] Will families in Kuwait do so? Will they have another

choice if genetic counselling were offered to them? Or will they find prenatal diagnosis and selective abortion unacceptable? Studied families will reveal some answers in the following sections.

7.4.6. Birth rank

Figure 16 Birth rank of first affected child among families who *wanted to delay* further pregnancies after diagnosis.



Birth rank of first affected child among families who *did not want to to delay* further pregnancies after diagnosis

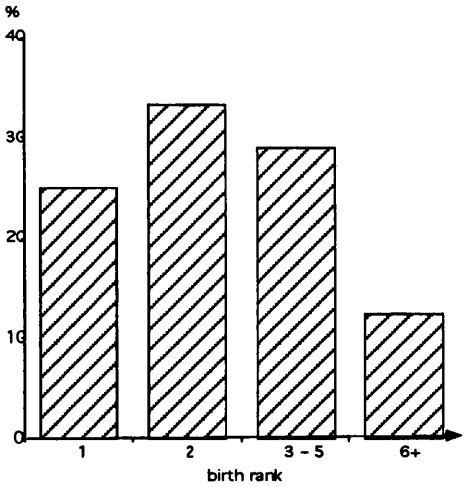


Figure 16 shows the influence of the birth rank of the first affected child on parents' reproductive behaviour. The first affected child was the first born in 50% of families who wanted to delay further pregnancies. If those families'

intention was accompanied by early diagnosis and counselling, the outcome of their reproductive behaviour could had been modified.

7.5. Consanguinity, screening before marriage and social impact of the disease

Consanguineous marriage has been a traditional deeply rooted custom in the Middle East. It is cultural rather than Islamic, for it is not stated anywhere in Islamic religion that consanguineous marriages are encouraged. Consanguineous marriage is characteristic of many aboriginal and tribal groups in the world, and it was shown that at least 20% of the world population favours consanguineous marriage, and at least 8.4% of all infants born are offspring of consanguineous parents.[82] Social benefits of this marriage are well known in Middle Eastern societies, they are well protected, supported and known to last. There have been no such studies from the Middle East which identify influence of the presence of inherited diseases on such marriages. Dr Darr's study[83] (1991) on British Pakistani families showed that consanguineous marriage was supported among the extended family in the presence of thalassaemia major: "None of the women were blamed for the disease", "there was not a single case in which a husband overruled his wife's decision on whether to terminate a pregnancy or not".[83] Parental consanguinity has genetic effects because it increases homozygosity and decreases heterozygosity in the offspring. It therefore increases the risk of recessively inherited disorders in the offspring.[82] When a recessive gene is common, for example SCD in Saudi Arabia (10 - 25%),[3] a carrier has a relatively high risk of marrying another however they choose their partner, and the risk is approximately doubled in a first cousin marriage.[82] Yet "The proportion of loci at which a person has inherited two copies of a gene from a common ancestor falls rapidly as relationships become more remote".[82]

The rate of consanguinity (first cousins) 61.6% (30.8%) in studied families was much higher than the known consanguinity rate 28% in Kuwait.[84] It is not surprising that *almost all (48 = 92%) parents were convinced that cousins' marriages imply increased risk of the disease*, because they had heard it repeatedly from their doctors: *"Are both of you blood related?" "Are you cousins?"*

But it is clear that this concept of consanguinity was misinformed or not well understood by parents. *The three divorces which this study reported among SCD parents were of consanguineous* marriages (a first cousin, a far cousin and a far relative). Although the question of "divorce" was not on the designed questionnaire, parents volunteered to speak about it. Two other families told about two divorces occurring among their relatives because of diagnosis of SCD child.

However, in all the three divorces among the 52 studied families, *women were blamed for the disease*. One husband admitted that he himself was a carrier only when he produced affected children of his second non-consanguineous marriage.

The rate of divorce among SCD parents in this study 5.7% is clearly higher than the rate known among Kuwaitis 1.7%[79]. It is most probably an underestimate because parents were not asked about it and only 3 of them disclosed. In spite of divorces, significant unawareness was obvious, especially amongst husbands who refused to be screened, chose the divorce and re-marriage, and produced more at risk children. This indeed shows how essential a genetic counselling is. Although all but one family claimed that they would advise their carrier daughter/son to tell her/his partner about it before marriage, this might not be translated into reality in the future.

Almost all 50 (96%) parents voted for "screening before marriage". They wanted it to be lawful for all couples not necessarily known to have a relative with SCD. They seemed to be more comfortable with such screening than with

disclosing to one another about it. At the same time parents proposed that in the presence of the custom of "arranged marriages", families have to disclose to each other about the carrier state of their youths who contemplate marriage. However, social taboos and stigmas of the disease clearly are well known in many societies,[14] and were avoided in the studied group. During conducting the project, no interviewed family told another about it, and no parent invited a relative or a friend to participate in the project. Families' high response to disclosure before marriage remains uncertain. Until a community genetic programme which screens for carriers is implemented, the solution seems to be by screening all members of the family of a diagnosed SCD child, and by counselling them.

7.6. Attitude to neonatal screening

Screening for sickle haemoglobinopathies could prove to be cost effective either because it reduces morbidity through early detection or reduces disease recurrence through genetic counselling. Aims of neonatal screening are mentioned in parents' own words in the Results Chapter. *Nearly all parents 50 (96%) voted to screen at birth.* Many of whom suffered because of delayed diagnosis, and produced more children successively carriers or affected before being informed about it. They wanted it mainly to plan for the affected child's medical and social care and for their own family future. However, in Jamaica, only 23% of mothers and 41% of SS women favoured diagnosis at birth when they were asked to choose between at birth or before birth.[47] The neonatal period is a sensitive time. Supporting parents and keeping in touch with them is necessary. They might need time to understand the information. The birth of an SCD child could be life threatening, disabling illness with its social implications, school absences, underachieving, and occupation limitation in the future. Although it had been reported that there was no increased mother's

tendency to over-protect her affected child after neonatal screening[30], differences in societies understanding and behaviour are expected. The efficiency of neonatal screening is proved only if it was associated with follow-up and counselling.[36,38]

7.7 Attitudes to prenatal diagnosis and termination

Advances in DNA technology[43,48] have permitted the antenatal diagnosis of a number of genetic diseases,[85] and these techniques have been widely applied in the detection of β thalassaemia[86] and SCD.[48] The β globin gene lies on a short arm of chromosome 11,[6] the synthesis of sickle Hb results from the substitution of valine for glutamic acid at β^6, and it is possible to detect the presence of sickle cell gene with very small amounts of DNA from any foetal source.[44,46] SCD is one of the several severe inherited disorders which cause mortalities, long periods of ill health, and require expensive, time consuming and often painful treatment. SCD causes not only physical disabilities but also social and family problems, not least because of the risk of further affected children. Antenatal diagnosis can reassure the family that a subsequent foetus has not inherited the disorder or give the option of termination if a foetus is found to be affected.[87] The prenatal diagnosis techniques became available before 12 weeks of pregnancy,[88] and have had a marked impact on the birth rate of β thalassaemia,[89] and are being increasingly used for the early detection of SCD.[87] It is therefore of interest to assess the attitudes of affected Kuwaiti families in order to determine whether these procedures should be made available in Kuwait.

• It is really interesting and encouraging that *38 (73%) families, all being Muslems, would accept prenatal diagnosis if it were offered to them. 12 of whom (31.5% of sample = 23% of total) would terminate pregnancy if they*

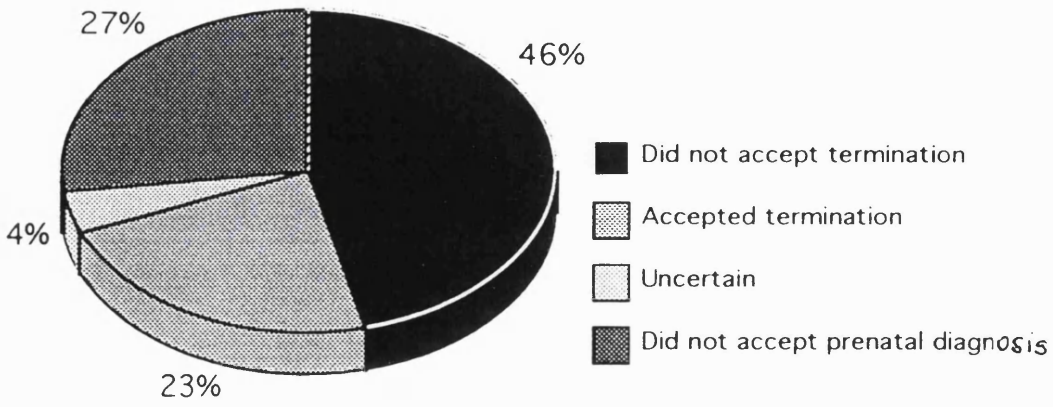
were faced with a diagnosis of an affected foetus. Two families were uncertain about it.

Acceptability of antenatal diagnosis in Jamaica (1988) among mothers (AS) of SS patients was 76%,[47] quite similar to this study's outcome of 73% acceptance, whereas among SS women there it was 58%.[47]

• The questionnaire made it clear to all interviewed families that antenatal diagnosis would be done before 12 weeks of gestation (in the first trimester). Therefore all the 31.5% who would terminate did in fact choose the first trimester method (chorionic villus sampling: CVS). Whereas 74% of all respondent women in Jamaica chose the CVS method rather than the amniocentesis of second trimester.[47] In the UK prenatal diagnosis was requested in 82% of pregnancies in which the mother was first seen before 13 weeks gestation and in 49% of those in the second trimester.[87]

Figure 17

The outcome of acceptance of prenatal diagnosis test and of termination of an affected foetus



• Approximately one third (31.5%) of families would terminate among those who would accept antenatal diagnosis. Which seems similar to its acceptance in Jamaica: 30% of female patients and 46% of mothers.[47] Considering the

cultural and the religious differences between SCD Kuwaiti families and those of Jamaica, the rather similar attitudes of the two groups shows that people from different parts of the world might think similarly and might accept same methods in terms of health and disease.

• In some centres foetal blood sampling for antenatal diagnosis was associated with 5% foetal loss,[43] whereas at the prenatal centre at UCH in London, CVS or foetal blood sampling are associated with 1 to 2% risk of miscarriage.[87] Parents who declined antenatal diagnosis were not asked about the reason, not only because it was such a sensitive issue to enquire about there, but also to leave a chance for a second step in approaching those families about it in the future. It was observed that parents hardly questioned the test safety, either because it was the first time that they had heard about it, or because of a mutual trust between them and the health services offered to them in Kuwait. Two mothers and one couple were concerned about the technique, and one said it would cause anxiety.

• Likewise it was not in the questionnaire to ask parents who would not accept termination of an affected foetus about the reason. Their discomfort about it was so obvious, and this is closely related to their religious and cultural belief. But it is clear that those who would not accept termination (26 = 68.5% of sample) would like to know the diagnosis of their foetus.

Therefore, it is not surprising that *only one couple amongst those who would terminate said "No, it is not against religion to do so"*. Whereas all other (11) families seemed to justify their option to terminate:

"Well, it might be against religion, if it were done when the foetus had its "Rouh"*

* Rouh is the soul

"Yes, it has been said it is against religion, but I have been suffering all my life", then she wept.

"It could be against religion, but Allah asked us to think".

"No, do you think it is against religion if it were done early?"

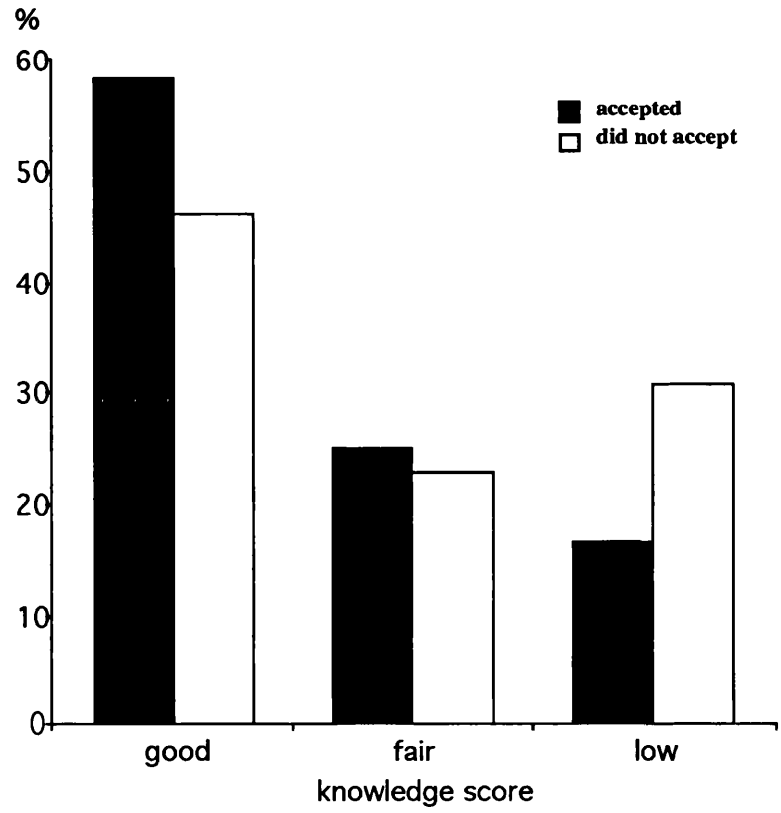
"Well, I am not entitled to say it is against religion or not, it needs a "Fatwa†", you know that, don't you?"

Meanwhile, where such services are well established, as in the UK, the uptake of prenatal diagnosis was 58% among couples at risk of SS disease, and about half of those at risk of the HbS/β thalassaemia.[87] Termination of an affected foetus occurred in 28/33 i.e. (85%).[87] It is also estimated that 8 cases of SCD could be prevented each year in both NW Thames and SW Thames in the UK.[90]

† Fatwa is legal islamic permissin.

Figure 18

Knowledge degree of families who accepted termination of pregnancy if the prenatal test were positive, and of families who did not accept.



• Although numbers are small, characteristics of parents who would accept termination of an affected foetus (figure 18 and table 20) show that they were more knowledgeable about the disease transmission, more educated and had higher incomes than those who did not accept termination. Therefore, in Kuwait, factors influencing SCD families' choice of an affected foetus are: Their knowledge about the disease, and their social standards in terms of education and of channels leading to information. These results together with the fact that all the respondents were conservative Muslems point to an important modification of thinking and of decision making in this society.

7.8 Ethical views

7.8.1. Termination of a homozygous SS foetus

Sickle cell disease represents a range of variable conditions of severity. The clinical course is markedly variable and "prediction of the nature of the clinical course currently almost impossible".[47] While in conditions such as homozygous β thalassaemia, severe clinical course of a child dependent on blood transfusion can be predicted, and genetic counselling is consequently easier to conduct, although the termination is always the parents' decision. In SS disease, parents faced with the diagnosis of their unborn children, get limited prognostic advice and ultimately rely on their personal experience of the disease. For example, in Jamaica, over one quarter considered that the disease was not sufficiently severe to justify termination,[47] whereas the proportion of mothers selecting antenatal diagnosis was 100% among those with a friend or relative dying with the disease, and only 61% of those mothers whose experience was a problem-free life with the disease.[47]

In this study, the clinical severity was not measured, and the parents' choice is therefore not to be related to their experience of the disease severity. Future studies in this respect should consider: Why the parents who would choose prenatal diagnosis would refuse termination of an SS foetus in the Arabian peninsula? Would it be influenced by their religious belief or by their experience with the disease?

Termination of an SS foetus is currently a widely held ethical dilemma.

• In general, loss of a foetus means loss of a baby. The psychological burden could be enormous, and supporting mothers after termination of pregnancy, via the counsellors, is necessary.

7.8.2. Permission for inducing abortion in Kuwait medical law

The medical law in Kuwait permits inducing abortion before four months of gestation only if it would cause serious ill health for the mother, or if it were proved that the foetus is severely physically malformed or severely mentally retarded, and these were incurable.[91] The procedure should be done (if not urgent) in a government hospital, and signed by a committee of three spectialists, one of whom at least should be an obstetrician / gynaecologist.[91] Inducing abortion for any other condition remains illegal.[91]

7.8.3 The rights of the foetus and abortion in Islamic religion

Ethics, law and religion are concerned with abortions that occur as a result of direct human intervention, whether self-inflicted or otherwise. These have religious, ethichal and legal implications.

Islam, like other religions, upholds the sanctity of life. Examples of verses in the Qur'an which testify to this: *"And do not take any human beings life - (the life) which Allah has willed to be sacred - otherwise than in (the pursuit of) justice".*

Hence, do not kill your children for fear of want (poverty): it is We Who shall provide sustenance for them as well as for you. Verily, killing them is a great sin".

7.8.3.a. The foetus

The word foetus is equivalent to the word "Janin" in the Arabic language, which would comprise anything that is inside the mother's womb from the time of conception till birth.[92]

The view of Imam al Shafi'i holds that the least stage whereby (that which is in the womb) could be called a foetus is that when the stages of "al mudghah" and "al'alaqah" have been differentiated, and it can clearly be made out to be of

human generation, possessing such characteristics as finger, or nail, or eye or anything else similar to that. Thus Imam Shafi'i definition of the foetus is closest to that of the present day scientific understanding. But it should be noted that Islamic law, like the Qur'an, refers to the procreated being inside the woman's body as "Janin" (foetus) irrespective of the stage of its development.[93-A] Islamic law upholds the right to life of the foetus, it is necessary to postpone the carrying out of the death sentence on a pregnant woman until after she has given birth and provisions having been made for the child to be suckled by a wet nurse.[93-A] The division of the heritage is requested to be postponed until after its birth. This shows that due consideration is taken of its existance.[94] Similar ethics are noted somewhere else. A new Danish law (1988) established an ethical council "the work of the council shall build on the basis that human life takes its beginning at the time of conception".[95]

7.8.3.b. Unwanted pregnancies in Islam

Islam teaches and encourages preventive measures to avoid such pregnancies. For example, the solution of "foetal alcohol syndrome" is made possible by Islam's prohibition of the intake of alcohol absolutely.[96] Prevention of genetically determined diseases is quoted here as it is mentioned by Ebrahim AFM, to help in providing the insight needed.[93-B]

"Carriers of genetic diseases"

"If it is established that the prospective partners are both carriers of a certain genetic disease and that their union may result in the transmission of that disease to their progeny, then some sort of counselling should be done to apprise them of the apparent risks involved. If both, in spite of that, are still willing to contract the marriage, then it may be wise for them to use contraceptive devices so as to safeguard against the conception of issues that would be stricken with the genetic disease. It may be emphasized here that Imam al-Ghazali makes a

clear distinction between contraception and abortion. If however, after taking all precautionary measures, deformed foetuses are detected, it would be best to consider that as a trial from the Almighty and practise patience, bearing in mind what the Qur'an says:

"Your riches and your children be but a trial ; but in the presence of Allah is the highest reward""[93-B]

7.8.3.c. Abortion in Islamic literature:

• Islamic schools maintain that at any stage after fertilisation has taken place, the zygote should not be disturbed. Interference with its development would be a crime.[93-C] However, Al Hanafi school permits abortion before the fourth month of pregnancy if it poses a threat to the life of an already existing infant belonging to the pregnant woman.[93-C] Others specify that abortion may be induced before the fourth month of pregnancy, if the mother's life is in danger, or if the pregnancy endangers the life of an existing infant being dependent on mother's milk for survival.[93-C] This is similar in part to the Medical Law in Kuwait.[91]

• Ibn-Sina, the famous Muslim physician (10th century) mentioned indications of abortion, which were for gynaecological reasons and to prevent mothers' ill health.[93-C]

• Al-Razi, another Muslim physician (9th century) described remedies which induce abortion.[97]

• The current British law under the terms of the Infant Life (Preservation) Act, accords with widespread moral intuitions that where the life of a pregnant woman is threatened by continuation of a pregnancy, abortion is justified.[98]

• Finally, this study's interest is to discuss views and not at all to find justification for terminating pregnancies of genetically affected foetuses. However recently in Iran, the medical law has been changed to permit early termination of foetuses affected by thalasseamia.[99]

8 Conclusions

Though prenatal diagnosis and neonatal detection programmes are well established, parents are now able to choose preventive measures for their genetically determined diseases, and as techniques for gene transfer and gene therapy are now on the horizon, sufferers from genetic diseases in my part of the world are still only able to receive treatment of their acute conditions and complications.

Affected families' views about SCD in Kuwait and their prospects for the future in terms of the present technology are examined, so as to establish a base for an appropriate genetic programme which fits those families' requirements.
I am not aware of any similar study on SCD in the Middle East especially in the Arabian peninsula.

Although numbers are small because of unpredicted events in 1990 in Kuwait, some interesting observations and useful results have come out of the research.

Although half of the studied parents had "good" knowledge about the genetic transmission of the disease, parents still require well designed qualitative information on the issues of the inheritance of SCD. They need to know about the implications, especially on the risk persistence in all pregnancies, and that recessive inheritance comes from both parents. In addition they need to understand what the presence of a carrier implies and about carrier mating.

Although the birth of an SCD child implies that there is an increased risk for other relatives of being carriers of the SCD gene, the hereditary aspect of the disease is not often discussed with relatives. There is still stigma attached to hereditary diseases. Very few parents were informed by a relative before they planned to

have children, and these did not believe it. This aspect should get more explicit attention from counsellors.
The sources of parents' information were mainly professional and no special attention was paid to the use of the mass media.

The best age for information transfer about the disease in the family was 15 years. Disclosure about who carried the trait between proposed partners was desired by parents.

Parents' reproductive behaviour was influenced by the family size and to some extent by their knowledge about the disease, rather than by their socio-economic conditions. Those who used contraceptive measures wanted to space pregnancies after diagnosis of an affected child rather than to limit the family size. Families' reproductive behaviour could have been modified if they were genetically counselled or if delayed diagnosis could have been prevented.

In the presence of a high rate of consanguineous (first cousin) marriages among the study families, great care should be taken in informing them about the disease transmission. The custom of consanguinity, which has advantages for that society, need not be broken, and parents should not be misinformed. The social burden on a divorced, blamed woman may be enormous, and can be avoided.

There is a high desire for screening among those parents, both for neonatal screening and for screening before marriage, which they strongly suggested should be made lawful. Almost three quarters would accept prenatal diagnosis if it were available in Kuwait, but only about one third would terminate an affected foetus.

9 Recommendations

9.1. Parents / patient - doctor relationship

a. The links between parents/patients and doctor need to be strengthened and maintained by follow up, and by devoting more time to listening and to explanation. All members of the family of an affected child should be screened and counselled where appropriate. The relationship should be built on clear understanding of the parents' agony and the burden of the disease on the family.

b. Analgesia for vaso-occlusive sickle pain should be given in adequate doses and freely available. Patients might be non-copers and manifest a high demand for analgesia. Many parents in this study complained bitterly about analgesia being insufficiently given because of the doctor's fear of inducing addiction to drugs.

c. Identification of the gene mutation, and proper diagnosis of the disease and of other genetic interactions which modify its manifestations is necessary before screening and counselling, not only for the patient and his family's sake, but also to enable health authorities to plan the appropriate health care.

9.2. Establishing a preventive genetic programme

The programme consists of close collaboration between doctors, representatives of the interested community and local health authorities. The primary objective is to promote genetic counselling and family planning for all sickle cell heterozygotes, with maximum respect for individual choices.

a. Provide accurate information to the population and to the health workers, making use of the mass media.

b. Establish a sickle cell disease society, whereby families, health and social workers can meet and exchange information.

c. Design a series of explanatory booklets and slides that can be used as teaching material at schools for 15 year old pupils, and involve teachers. Other booklets and videos could aim to educate parents.

d. Train a group of interested, well informed individuals in genetic counselling which respects cultural, religious and economic factors of an affected family.

e. Community screening for the carriers, and screening at birth. There is an urgent need for a good epidemiological study of SCD in Kuwait to find the prevalence and the gene frequency, this would be most effective by neonatal screening.

9.3. Re-evaluate affected families' knowledge after councelling to find out whether they have changed their social and reproductive behaviour, and whether they opted for screening as was found in the study.

9.4. Further studies into the psycho-social impact of the disease on patients and their families are needed.

9.5. Before implementing the antenatal diagnosis, a larger conclusive study on the need and acceptability of the test is necessary to predict whether the introduction of this test to Kuwait with the offer of termination of affected pregnancies may have an effect on the birth rate of affected children with SCD or not.

9.6. The status of prenatal tests depends on whether termination of affected pregnancies is allowed. There is still a dispute about the permissibility of termination in Kuwait and other countries in the Middle East. However, prenatal tests select the pregnant mother as a target for prevention of the disease. The risk of miscarriage and the burden on the mother's health, however minimal, should be taken into account. There is help in the recently documented literature on pre-implantation diagnosis of SCD and on gene transfer therapy which suggests that prevention and cure is possible, at least for those who can afford it.

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Appendix 1

1. The Questionnaire

A CHILD WITH SICKLE CELL ANAEMIA : PARENTAL KNOWLEDGE ABOUT THE GENETIC TRANSMISSION AND THEIR ATTITUDES TOWARDS SCREENING

		Coding	Variables
Name of the Child :			
Serial No.	(.....)	(.....)	CODE NO
1. Interview given by :		(.....)	INT.BY
Mother 1	(.....)		
Father 2	(.....)		
Both 3	(.....)		
2. Age / Year			
Mother 1	(.....)	(.....)	MO.AGE/YR
Father 2	(.....)	(.....)	FA.AGE/YR
3. Patient interview at :		(.....)	INT.AT.
Hospital 1	(.....)		
Clinic 2	(.....)		
Home 3	(.....)		
4. Country of Origin (Father) :		(.....)	FA.ORIGIN
Kuwait 1	(.....)		
Palestine 2	(.....)		
Iraq 3	(.....)		
Iran 4	(.....)		
Egypt 5	(.....)		
Saudi Arabia 6	(.....)		
Lebanon 7	(.....)		
Syria 8			
4.b. Nationality :		(.....)	NATION
5. Address : ..... Tel. No.			
Area of Residence :			

	Coding	Variables
Area of Residence : (.....)	(.....)	AREA

1. Jahra	12. Salmiya	22. Faiha
2. Nugra	13. Sulaibikhat	23. Shamiya
3. Farwaniya	14. Salwa	24. Mansouriya
4. Khaitan	15. Qadsiya	25. Mishref
5. Omariya	16. Daiya	26. Rawda
6. Rigga	17. Bayan	27. Al Dahya
7. Fintas	18. Jabriya	28. Kaifan
8. Hawalli	19. Yarmouk	29. Qurtoba
9. Rumaithiya	20. Ahmadi	30. Dasma
10. Adailiya	21. Shaab	31. Nuzha
11. Failaka		32. Khaldiya

6. Socioeconomic Status :

Education of Mother			(.....)	EDU_MO
Post graduate	1	(.....)		
College	2	(.....)		
High School	3	(.....)		
Elementary School	4	(.....)		
Less	5	(.....)		
Education of Father			(.....)	EDU_FA
Post graduate	1	(.....)		
College	2	(.....)		
High School	3	(.....)		
Elementary School	4	(.....)		
Less	5	(.....)		
8. Family Income :			(.....)	INCOME
(KD/Year) > 35,000	1	(.....)		
20,000 - 35,000	2	(.....)		
10,000 - 20,000	3	(.....)		
3,500 - 10,000	4	(.....)		
< 3,500	5	(.....)		

	Coding	Variables
9. Age of Affected Child (index child) D.O.B. in years	(.....)	AGE_AFF.YR.
0. His/Her position in the family 1st 1 2nd 2 3rd 3 4th 4 more 5 specify	(.....)	POSITION
1. Age at onset symptoms :	(.....)	AGE_ONS.YR
12 Age at diagnosis :	(.....)	AGE_DIAG.
13. Has the child been admitted to hospital because of these symptoms*.....Yes 1 (.....) No 2 (.....)	(.....)	ADMITTED
14. If Yes : a. age at first admission 1 (.....) b. How frequent : 2 (.....) b1. every 1 month (.....) b2. every 3 months (.....) b3. every 6 months (.....) b4. every 12 months (.....) b5. less frequent (.....)	(.....)	AD.AGE AD. FRE
15. Has the child been admitted to hospital because of other reasons : Yes 1 (.....) No 2 (.....)	(.....)	AD.OTH.RE/
16. When was it first to know about an effected child: a) When this child was diagnosed (.....) b) When an elder child was diagnosed(.....)	(.....)	F/R. KNOW
17. Where was the information about the diagnosis given : in a hospital ward 1 (.....) at a hosp.outpatient 2 (.....) at a polyclinic 3 (.....) other, specify 4 (.....)	(.....)	INFORM

* Symptoms are those of Sickle Cell Anaemia crises like abdominal pain, joints and limbs pain, chest pain etc ... and of haemolysis.

	Coding	Variable
18. Who gave the information about the disease :	(.....)	WH.INFOR
A paediatrician 1 (.....)		
A haematologist 2 (.....)		
A genetist 3 (.....)		
Another, specify 4 (.....)		
19. Was the disease explained in the presence of :	(.....)	EXPLAIN
Father alone 1 (.....)		
Mother alone 2 (.....)		
Both together 3 (.....)		
20. Did you try to look for information somewhere else :	(.....)	INF.SM_W
Yes 1 (.....)		
No 2 (.....)		
21. If yes, where :	(.....)	IFY.WH.
a) travelling abroad for further medical advice or treatment 1 (.....)		
b) You had a chance to read a leaflet about the disease 2 (.....)		
c) A parent who had a similarly affected child 3 (.....)		
d) From T.V. or newspapers 4 (-----)		
22. How many children do you have (.....)	(.....)	CH.NO
23. Do you intend to have more children	(.....)	M.CHI.
yes 1 (.....)		
No 2 (.....)		
24. Did you want to delay further pregnancies after the affected child was diagnosed	(.....)	D.PREG.
yes 1 (.....)		
No 2 (.....)		

	Coding	Variable
18. Who gave the information about the disease :	(.....)	WH.INFOI
A paediatrician 1 (.....)		
A haematologist 2 (.....)		
A genetist 3 (.....)		
Another, specify 4 (.....)		
19. Was the disease explained in the presence of :	(.....)	EXPLAIN
Father alone 1 (.....)		
Mother alone 2 (.....)		
Both together 3 (.....)		
20. Did you try to look for information somewhere else :	(.....)	INF.SM_W
Yes 1 (.....)		
No 2 (.....)		
21. If yes, where :	(.....)	IFY.WH.
a) travelling abroad for further medical advice or treatment 1 (.....)		
b) You had a chance to read a leaflet about the disease 2 (.....)		
c) A parent who had a similarly affected child 3 (.....)		
d) From T.V. or newspapers 4 (-----)		
22. How many children do you have (.....)	(.....)	CH.NO
23. Do you intend to have more children	(.....)	M.CHI.
yes 1 (.....)		
No 2 (.....)		
24. Did you want to delay further pregnancies after the affected child was diagnosed	(.....)	D.PREG.
yes 1 (.....)		
No 2 (.....)		

	Coding	Variables
5. If yes, could you actually delay further pregnancies yes 1 (.....) No 2 (.....)	(.....)	AC.D.PREG.
6. If Yes, by what method a) pills 1 (.....) b) Intrauterine device 2 (.....) c) Safe period 3 (.....)	(.....)	METHOD
7. If No, why : a) because you were hopeful for another healthy child 1 (.....) b) because you did not have mutual agreement with your wife/husband 2 (.....) c) because you believe human beings should accept their faith 3 (.....) d) because you've had enough children 4 (.....)	(.....)	D.PREG.WH.
8. How many pregnancies occured after the First affected child was diagnosed (.....)	(.....)	PREG.AF.DIAG
9. D.O.B. of each child/outcome of each pregnancy : Position D.O.B.		

* Average birth interval before diagnosis (in months)
* Average birth interval after diagnosis (in months)

	Coding	Varaibles
). Have you lost any child	(.....)	LAST
yes 1 (.....)		
No 2 (.....)		
1. If Yes, was the loss related to diagnosis	(.....)	L.REL.DIAS
yes 1 (.....)		
no 2 (.....)		
2. Parents :	(.....)	PARENTS
consanguinous 1 (.....)		
1st cousin 2 (.....)		
far relative 3 (.....)		
nonconsanguinous 4 (.....)		
3. Do you know of a relative affected by Sickle Cell anaemia	(.....)	RE.AFF.S.C
a parent 1 (.....)		
a brother, a sister 2 (.....)		
a niece/nephew 3 (.....)		
uncle/aunt 4 (.....)		
another 5 (.....)		
No 0 (.....)		
4. If yes, was it before you had had planned to have the affected child :	(.....)	PL.AFF.CHI
yes 1 (.....)		
no 2 (.....)		
5. If yes : Did any one suggest to you at that time that your child could be similarly affected	(.....)	SUG.AFFECT
yes 1 (.....)		
no 2 (.....)		

	Coding	Variab
36. Do you have :	(.....)	CARD
haemoglobinopathy card 1 (.....)		
a hospital card 2 (.....)		
no card at all 3 (.....)		
37. Do you think the Sickle Cell Anaemia that your child has is a serious illness	(.....)	SER.IL
yes 1 (.....)		
no 2 (.....)		
38. If Yes, why : (answer only one)	(.....)	IF.Y.S.
a) because s/he is not growing well 1 (.....)		
b) because s/he is almost ill 2 (.....)		
c) because s/he had many admissions to hospital 3 (.....)		
d) because you are not certain of his future 4 (.....)		
e) All the above 5 (.....)		
39. Have you been told what causes Sickle Cell Anaemia (answer only one)	(.....)	CAUSE
a) An infection 1 (.....)		
b) An illness in the mother during pregnancy 2 (.....)		
c) An inherited factor 3 (.....)		
d) An unknown factor 4 (.....)		
e) Child not eating well 5 (.....)		
Those who answer (c) proceed to 40 otherwise go to 41		
40. Have you been told how it is transmitted : (answer only one)	(.....)	TRANS
a) from mother alone 1 (.....)		
b) from father alone 2 (.....)		
c) from both 3 (.....)		
d) Neither from mother nor father 4 (.....)		

	Coding	Variabl
41. Have you been told whether Sickle Cell Anaemia is caused by an inherited factor yes 1 (.....) no 2 (.....)	(.....)	C.INH.F
42. Have you been told whether Sickle Cell Anaemia a) affects boys more than girls 1 (.....) b) affects boys and girls equally 2 (.....) c) Do not know 3 (.....)	(.....)	AFFECT
43. Have blood tests been done on your other children after diagnosis of the affected child : Yes 1 (.....) no 2 (.....)	(.....)	B.TEST
44. Have you been aware if any of your children can pass on the disease to his/her children yes 1 (.....) no 2 (.....) If Yes, go to questions : 45 - 50 If No, go to question : 51	(.....)	PASS
45. Have you been told whether this child (who has the risk of passing the disease) will be very ill 1 (.....) will stay healthy 2 (.....)	(.....)	V.ILL.
46. Do you intend to explain to your child (who may pass the disease) about the disease : yes 1 (.....) no 2 (.....)	(.....)	EXPL
47. If Yes : Do you intend to explain : a) only to boys 1 (.....) b) only to girls 2 (.....) c) to both 3 (.....)	(.....)	IN.EXP

	Coding	Variab
48. At what age would this best be done :	(.....)	B.DONE
10 years 1 (.....)		
15 years 2 (.....)		
20 years 3 (.....)		
just vefore marriage 4 (.....)		
49. If No, why : (answer only one)	(.....)	W.N.E)
a) because you do not want your child to worry 1 (.....)		
b) because you do not think you would influence the child behaviour in the future 2 (.....)		
c) because you think there is novreason to do so 3 (.....)		
50. Would you advice him/her to tell his/her partner about the disease before they marry or have children	(.....)	AD.PAI
yes 1 (.....)		
no 2 (.....)		
51. If No. why : (answer one)	(.....)	N.AD.:
a) because you prefer not to know about it 1 (.....)		
b) because it would not change future plans 2 (.....)		
c) because you have not heard about it 3 (.....)		
52. After having an affected child, have you been told	(.....)	OTH.C
a) it is likely that all your other children will be affected 1 (.....)		
b) some may be affected 2 (.....)		
c) unlikely that any of the others will be affected 3 (.....)		
d) have no idea 4 (.....)		

	Coding	Vari
53. Have you been told whether the chance of having an affected child :	(.....)	CH.A
a) persists in each pregnancy 1 (.....)		
b) disappears once you have an affected child 2 (.....)		
c) do not know 3 (.....)		
54. How do you think Sickle Cell Anaemia will be reduced : (answer only one)	(.....)	REDU
a) by screening partners before marriage 1 (.....)		
b) by giving repeated blood transfusions 2 (.....)		
c) by giving vitamins and drugs 3 (.....)		
55. Do you think there is a higher risk of Sickle Cell Anaemia if you marry your cousin :	(.....)	H.RI
yes 1 (.....)		
no 2 (.....)		
56. If there were a test in Kuwait which could tell you (by a drop of blood, nn the first week of life) whether your baby is affected or is a carrier, would you accept it if it were offered to you	(.....)	K.TI
yes 1 (.....)		
no 2 (.....)		
57. If there were a special test in Kuwait which could tell you whether your foetus (in the first few weeks of pregnancy) is likely to have the disease, would you accept it if it were offered to you :	(.....)	FOE
yes 1 (.....)		
no 2 (.....)		

	Coding	Variab
58. If Yes : if the test were positive would you want to carry on with pregnancy :	(.....)	C.PREG.
yes 1 (.....)		
no 2 (.....)		
uncertain 3 (.....)		
59. Year File opened (.....)		
60. Type of Hb. of index child :		
AS 1 (.....)	(.....)	Hb. Typ
SS 2 (.....)		
SF 3 (.....)		
SC 4 (.....)		
AC 5 (.....)		

Appendix 2

1.1 Kuwait the country:

Kuwait is an Arab country, in the North Eastern Arabian peninsula. It is bordered on the North and North West by Iraq, on the East by the Arabian gulf, and on the South by Saudi Arabia. It covers an area of 17818 sq. km between 28° and 30° North of the equator and between 46° and 48° east of the Greenwich meridian.[100] In summer it is among the hottest capitals in the world with high humidity in late summer, while in winter temperature minimum approaches freezing point.

Rainfall does not usually exceed 200 mm annually. As regards water supply, large sea water distillation plants were construced since 1953, there are several large sea water distillation plants, which produce more than 144 million gallons of fresh water daily, meanwhile natural fresh water was discovered at Rawdhatain in Northern Kuwait in 1960 and is distributed by pipelines to the houses for irrigation.[101]

The capital major city and commercial centre of the state is the city of Kuwait "Madina", which together with its suburbs is a modern city. The most densely populated region of the country was an area of 830 square kilometres, with population density 2638/sq km.[79]

1.2. The Population

In 1938 the position of the first oil field was located near Al-Ahmadi at Burgan[102]. Commercial production and export of oil began in 1946. In 1950 the Kuwait Development board was set up. Declaration of National Sovereignty was in 1961.[103] In the early 1950s the population was about

100,000. When the first population census was conducted in 1957 the population had doubled to 206,000.[79] Since 1957, a census of the population in Kuwait has been conducted every five years. The 1985 population census indicates that the population was 1,697,301.[79] Statistics from the General Assembly for Civil Information[74] indicated that the population had risen at the year 1989 to 2,014,135; 550,181 of whom were Kuwaitis.[74] Almost half (48.6%) of the Kuwaitis were aged less than 15 years in 1985, whereas only 29% of the non-Kuwaitis were in this age group.[79]

1.3. Population Growth

The 1985 population census indicates a decrease in the annual growth rate of the population of Kuwait to 4.5% for the intercensal years 1980-1985, compared with 6.4% between the census of 1975 and 1980.[74] The 1985 census figures indicate that the rate of growth for the Kuwaitis remained unchanged at 3.7% compared with a decline in that of the non-Kuwaiti population by 5.1% against 8.7% between the census of 1975 and 1980.[74] With the exception of the period between the 1970 and 1975 censuses, the rate of growth for non-Kuwaitis since 1957 was higher than that for Kuwaitis. It is clear that this is attributable to the high rate of immigration, which is considered to be the main factor responsible for the increase in the Kuwait population.

Kuwait is one of the fast developing nations, and is a centre of world importance. More than half of its community were expatriates from less affluent nations. Until 1990 Kuwait housed more than 120 different nationalities,[101] among whom Arabs predominated, they were mainly Palestinians, Egyptians, Iraqis and from other Arab countries. Among non-Arab countries, Indians, Pakistanis and Iranians predominated the Asian nationalities, there were other nationalities from Africa, Europe, North and South America.

In the late 1980s, immigrants from South East Asia were attracted by jobs in government establishments, the private sector and in households. This vast influx not only increased the total size of the community, but also lead to social and health problems by importing communicable and non-communicable diseases to the community.[101]

1.4. Health Services

Health services in Kuwait have been totally sponsored by the government, and equally provided to both Kuwaitis and non-Kuwaitis living in Kuwait. Recently, although to some extent limited, the private medical sector has developed. Medical services comprised all essential and updated centres, such as preventive health sector, family health, organ transplant, nuclear medicine, cancer centre, and other specialities and sub-specialities. Provision of health care followed a strategy which started with the GP or family doctor in a regional clinic (or a polyclinic where other main specialities existed) and passed through a regional hospital or a speciality hospital. In 1980s, the population-doctor and population-nurse ratio for Kuwait was 570 and 180 respectively[79]. While in China and India it was 1,858 and 3,279, and among High Income oil expatriates it was 1,360 and 836.[79] Here are some health indicators of Kuwait, which compare quite favourably with the levels for developed countries (USA in an example). Egypt and Jordan are examples of other Middle Eastern countries.[104]

Table 21 Health indicators of Kuwait compared to other countries

The health indicator	Kuwait	USA	Egypt	Jordan
Life expectancy at birth 1991	75	76	61	67
Under - 5 mortality rate 1960	128	30	260	180
Under - 5 mortality rate 1991	17	11	85	46
% of population with access to health services 1985 - 1988	100	. .	. .	97
Contraceptive prevalence % 1980 -92	. .	74	38	35
Maternal mortality rate 1980 -90	6	8	320	48
% of Central government expenditure allocated to health 1986-91	8	14	3	6

From the State of the World's Children, UNICEF 1993.[104]

1.5. The Haematology Unit in the Paediatric Department of Sabah Hospital

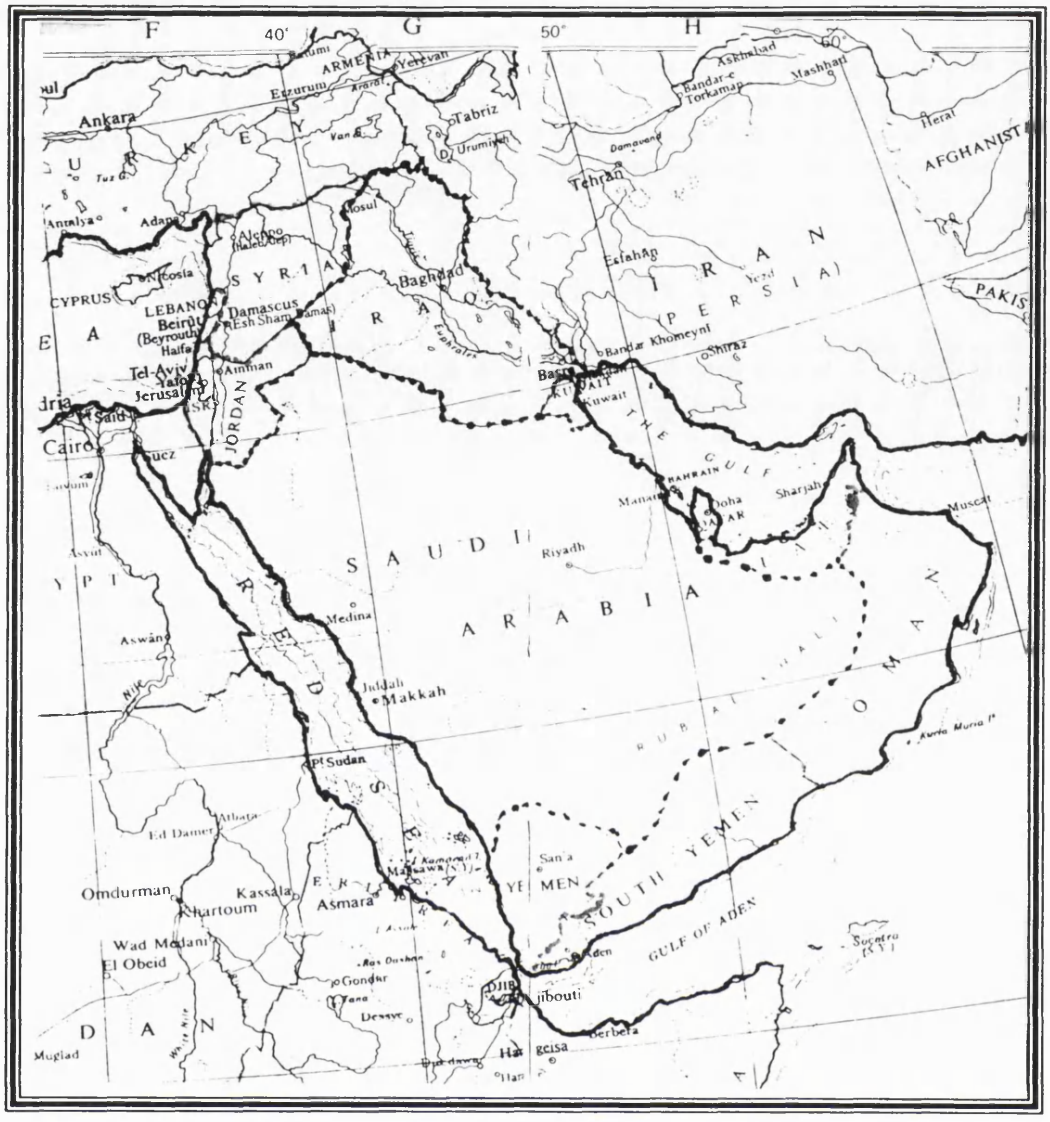
Sabah Hospital was constructed and health services started in 1963, when at the time it was the largest hospital in the Middle East. It took the main load of treating patients from all over the country until regional hospitals started in the late 1970s. There were 3 main constructions: general medicine department, general surgery, and paediatrics. New buildings together with changes and reforms helped to extend medical services and to include many other specialities. The capacity of the paediatric department was 252 patients, divided into 9 wards, one of which is Paediatric ICU.[105]

The Haematology Unit was set up in 1973. Its main concern was Haemoglobinopathies patients. In 1975 Leukaemia patients management was started by a multi-disciplinary team from the cancer centre, haematology

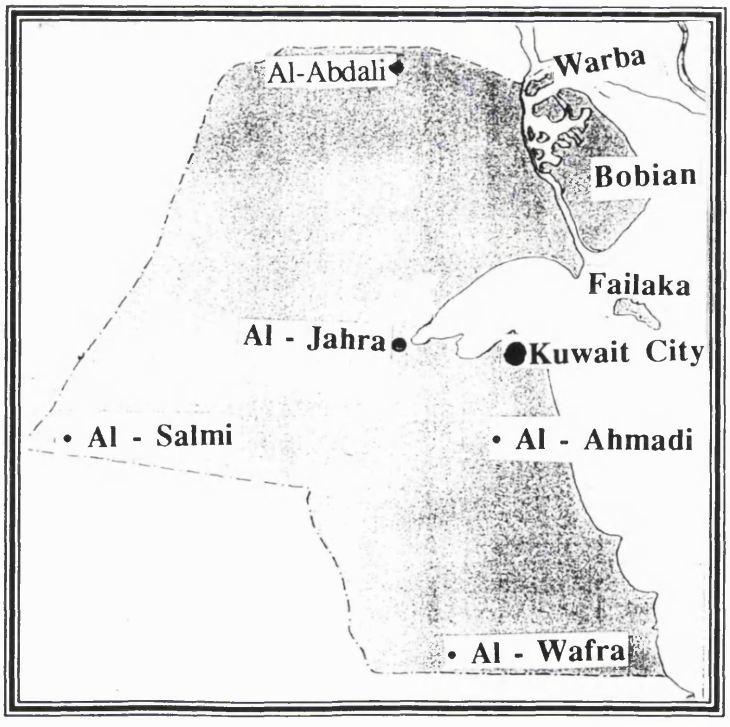
laboratory, and paediatrics. In 1989-90 one ward was allocated for patients with thalassaemia, who were under regular follow up.[105] Two clinics were held weekly one for leukaemia and one for other blood diseases.

Sickle Cell Anaemia patients were thoroughly investigated on arrival at the Unit. Their parents and other offsprings were usually screened for SCD as well. But those SCD patients were not under regular follow up.[105]

Middle East



Kuwait



Appendix 3

1. Arabic translation of the Brent sickle cell centre leaflet

Appendix 3

1. Arabic translation of the Brent sickle cell centre leaflet

-(ماهـــو فقـــر الـــــــدم)-

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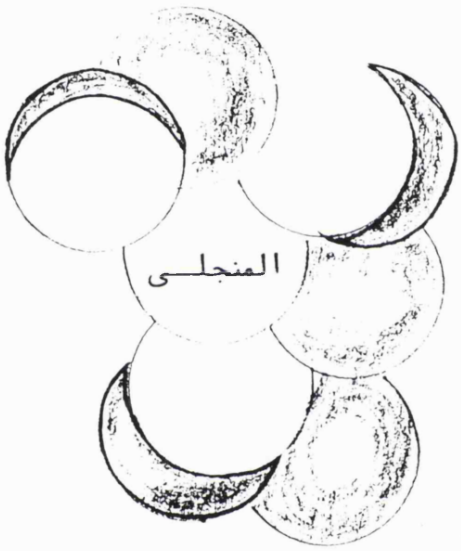


ما هـو المـرض المنجلـى ..... ؟

من هـو الحامـل لهذا المـــــــرض ؟

****

****

ما هو فقر الدم المنجلى ؟

انه أحد الأمراض التى تصيب الهيموجلوبين داخل كريات الدم الحمراء .. والهيموجلوبين هو المادة التى تحمل الأكسجين فى الكريات الحمراء ، وتنقله من الرئتين الى جميع أنحاء الجسم ، وكذلك هو المادة التى تعطى الكريات لونها الأحمر ...

وراثة الهيموجلوبين :

كيف تنتقل صفات الهيموجلوبين من الوالدين الى الأبناء ؟: ان كل واحد منا يرث نوع الهيموجلوبين عن أبويه بواسطة زوج من " العوامل الوراثية " أى " الجينات الوراثيه " .. وتختص هذه الجينات بجميع صفاتنا الوراثيه ، مثل شكل الأنف ولون العينين ..

ان أكثر أنواع الهيموجلوبين شيوعا بين الناس ، هو النوع المعروف بهيموجلوبين AA (وحرف A مأخوذ من كلمة Adult فى اللغة الانجليزية) ولكن هناك أنواع أخرى كثيره ...

وهنا نود التنبيه الى أن نوع الهيموجلوبين شئ يختلف تماما عن فصيلة الدم .. هذه الصفحات توضح لنا أنواع الهيموجلوبين التى تحدث فى فقر الدم المنجلى ...

المرض المنجلى Sickle Cell Disease :

فقر الدم المنجلى هو أحد أنواع " المرض المنجلى " ، التى تحتوى أيضا على مرض " SC " ومرض " فقر دم حوض البحر المتوسط المنجلى " (S-Beta Thal) وهذان الأخيران أخف شده من " فقر الدم المنجلى " ..

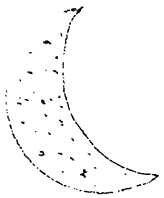
ومما هو جدير بالذكر أن المرض المنجلى غير معد ...

يتبع/ ....

فقـــر الـــدم المنجلـــى Sickle Cell Anaemia

عند ما يولد الانسان مصابابفقر الدم المنجلى ، فانه يكون قد ورث "الجـــين الوراثـــى" أى " العامل الوراثـــى" للهيموجلوبين المنجلى من والديه كليهما . . وعنـــد حدوث حالات معيّنـــة ، كنقص السوائـــل فى الجسم ، أو وجود عدوى أو التهـــاب ، أو وجود مادة التخدير التى تعطى عند اجراء العمليات الجراحية ، أو فى جالة الحمل، فان كريـــات الدم الحمـــراء المحتويه على الهيموجلوبين المنجلى ، تغـيّر شكلهـا مـــن الشكل الكروى المستديـــر الى الشكل المنجلـى (الذى يشبه المنجل) كما هـــو مبـــين بالرســـم . . .

كـــرة الدم الحمـــراء
الطبيعيـــه



كـــرة الدم الحمـــراء
المنجليـــه

وباستطاعة هذه الكريات المنجليه غير الطبيعيه أن تتجمع معا مكونه انســـدادا لمجرى الدم فى الأوعية الدموية الصغـيرة . . وهذا من شأنه أن يؤدى الى آلام فـــى مختلف أنحاء الجسم ، كالعظام أو البطن ، وفى بعض الأحيان ، يسبب التعـــب والاعيـــاء نتيجـة لفقر الدم . . ويتفاوت تكـرار هذه الآلام وشدّتها ، وحدوث المشاكل الأخرى ، من شخص الى آخـــر . . كما أن ذلك يعتمد أيضا على نوع المرض المنجلـــى المـــوروث . . .

مـــرض SC المنجلـــى (SC Diease) :

عند ما يولد انسـان مصابا بمرض " SC " المنجلى ، فانه يكون قد ورث الهيموجلوبين المسمّـى بهيموجلوبين " S " من أحد والديه ، ويكون قد ورث الهيموجلوبين المسمـــى بهيموجلوبين " C " من والده الآخر . . وهذا النوع يعتبر خفيف الشـدة بين أنـــواع المـرض المنجلـــى . . .

عند ما يولد انسان مصابا بهذا المرض ، فانه يكون قد ورث الهيموجلوبين المنجلى ، أى هيموجلوبين " S " من أحد والديه ، ويكون أيضا قد ورث عاملا وراثيا "لفقر د م حوض البحر المتوسط" من والده الآخر ...

ويختلف هذا المرض فى شدّته ، فقد يكون طفيفا وقد يشبه مرض فقر الدم المنجلى فى شدّته ..

أين تكثر الاصابة بهذا المرض المنجلى ؟

تكثر الاصابة بهذا المرض فى افريقيا والبحر الكاريبى ، حيث يوجد فى واحد من كل ٣٠٠ شخص ، كما أنه يوجد أيضا فى منطقة البحر الأبيض المتوسط ، وفى الآسيويين ، وفى البلاد العربية ولذلك ، من الأفضل أن نعرف نسبة حدوثه فى بلادنا ...

لماذا يوجد الهيموجلوبين المنجلى (هيموجلوبين S) فى الناس فى المناطق الحارة ؟

فى الماضى كانت الملاريا المتوطنة فى تلك البلاد ، تفتك بكثير من الأطفال .. غير أن الأطفال " الحاملين" لفقر الدم المنجلى ، استطاعوا البقاء ، وذلك لتمتّعهم ببعض الحصانة ضد أشدّ أنواع الملاريا .. ولسبب مازال غير معروف ، فان الملاريا لاتفتك بالأطفال" الحاملين" لفقر الدم المنجلى .. لذلك فان سلالاتهم يعيشون فى مختلف أنحاء العالم ...

ما معنى الحامل للمرض ؟

يرث بعض الناس جينا وراثيا للهيموجلوبين الطبيعى (هيموجلوبين A) من أحد والديه ، ويرث من والده الآخر جينا وراثيا لنوع آخر للهيموجلوبين مثل " S " أو " C " أو "حوض البحر المتوسط " ...

وهذه الحالة تعرض بالحامل للمرض ، فمثلا يسمى الحامل للمرض المنجلى هيموجلوبين " AS " ، ويسمى الحامل للهيموجلوبين "C " : " AC" ، ونذكر هنا بعض الأمثلة على حالات حمل المرض ، وكذلك نسبة حدوثها فى مجموعات مختلفة

من الناس . . .

الحامل للمرض المنجلى (هيموجلوبين AS) :

تبلغ نسبة الحاملين لهذا المرض ، لذوى الأصول الافريقية والكاريبيه واحدا بين كل عشره أشخاص ، أما فى نيجيريا فان النسبة أكبر من ذلك . .

الحامل لهيموجلوبين AC :

ان واحدا من كل خمسين شخصا من ذوى الأصول الافروكاريبيه ، يحمل هذا المرض ، وتزيد هذه النسبة عن ذلك فى غانا ، أما فيما يتعلق بفقر دم حوض البحر المتوسط ، فان شخصا واحدا من كل خمسين من ذوى الأصول الأفروكاريبيه يعتبر حاملا لهذا المرض ، وتزداد هذه النسبة فى مناطق البحر المتوسط وآسيا . .

تنبيهات هامه :

اذا كنت حاملا لأحد هذه الأمراض :

* فان ذلك لا يعنى أنك مريض به . . .
* ولا يعنى أنه معد أبدا . . .
* انه لن يتحول الى المرض المنجلى أو الى فقر دم حوض البحر المتوسط . . .
* ولكن اذا كنت أنت وشريك حياتك ، حاملين للهيموجلوبين المنجلى ، فان هناك فرصه لأن يرث أطفالكما المرض المنجلى نفسه . . .

كيف يصبح الانسان حاملا للمرض المنجلى ؟ هيموجلوبين " AS " :

يحدث هذا عندما يرث أحد نا الجين (أو العامل) الوراثى للهيموجلوبين الطبيعى (A) من أحد والديه ، ويرث الجين الآخر للهيموجلوبين المنجلى (S) من والده الآخر . . .

فاذا كان الوالدان كلاهما حاملين للهيموجلوبين المنجلى فان فرصة حدوث المرض المنجلى نفسه " SS " عند تكون كل جنين تكون ٢٥ ٪ أى ١ الى ٤ . . .

وهنا يجب أن ننبّه الى حقيقة هامه ، وهى أن كل طفل سيولد لهذين الأبوين ، يحتمل اصابته بهذا المرض بنسبة ٢٥ ٪ ..

كيف يصبح الانسان حاملا لهيموجلوبين "C" ؟

يحدث هذا عندما يرث أحدنا الجين (أو العامل) الوراثى للهيموجلوبين الطبيعى " A " من أحد والديه ، ويرث الجين الوراثى لهيموجلوبين" C " من والده الآخر .. فاذا كان أحد الوالدين حاملا للهيموجلوبين المنجلى" S " ، وكان الآخر حاملا لهيموجلوبين " C " فان فرصة حدوث مرض " SC " عند تكّون كل جنين تكون ٢٥ ٪ أى ١ الى ٤ ..

كيف يمكن لأحدنا أن يكون حاملا لأنيميا (أو فقر دم) حوض البحر المتوسط :

يحدث هذا عندما يرث الانسان جينا وراثيا للهيموجلوبين الطبيعى " A " من أحد والديه ، ويرث جينا وراثيا لأنيميا حوض البحر المتوسط من والده الآخر ...

ان أنيميا حوض البحر المتوسط تتسبّب فى انتاج كمية غير كافيه من هيموجلوبين الدم ، فاذا ورث طفل هذه الأنيميا من كلا الوالدين ، فانه يكون قد ورث مرضا شديدا (الأنيميا العظمى) المعروف بفقر دم حوض البحر المتوسط ..

اذا حدث أن أحد الوالدين حامل للمرض المنجلى ، والآخر حامل لأنيميا حوض البحر المتوسط ، فان فرصة كل جنين أن يكون مصابا بأنيميا حوض البحر المتوسط المنجلية (S-Thal) ، تكون ٢٥ ٪ ، أى ١ الى ٤ ..

* " لو حدث أن كلينا حامل للمرض المنجلى ، فهل يجب أن يولد كل أطفالنا بالمرض المنجلى ؟ "

- ذلك ليس حتميا ، ففى كل مرة يتكون لكما فيها طفل ، تكون هناك فرصة ٢٥ ٪ أى ١ الى ٤ ، أن يرث الطفل المرض المنجلى أو أن يرث الهيموجلوبين الطبيعى ،

كذلك فان هناك فرصة ٥٠٪ أى ١ الى ٢ ، أن يكون الطفل حاملا للمرض المنجلى ..

* " ماذا يحدث لو كان أحدنا نحن الوالدين ، حاملا للهيموجلوبين المنجلى ، والآخر طبيعيا ؟ " ...

- فى هذه الحالة ، امّا أن يرث أطفالكما صفة الحامل للهيموجلوبين المنجلى أو الصفة الطبيعيه ، ولكن لن يرثوا المرض المنجلى نفسه ...

* " كيف نستطيع معرفة اذا كنا حاملين للمرض المنجلى أو مصابين به " ؟

- هناك فحص خاص ، يجرى بأخذ عينه صغيره من الدم ، ويجرى هذا الفحص قبل العمليات الجراحية وفى عيادات الأسنان وخلال مدة الحمل ، اذ أنه من المهم جدا أن نعرف اذا كان الشخص مصابا بالمرض المنجلى ، قبل اعطاء التخدير اللازم للعمليات الجراحية ...

عندئذ يفحص هيموجلوبين الدم فى المختبر ، لمعرفة نوعه ، كالهيموجلوبين المنجلى وأنواع الهيموجلوبين الأخرى ...

كما أنه من الممكن فحص الطفل الوليد عند ولادته ، بحثا عن المرض المنجلى وأنيميا حوض البحر المتوسط .. وفى بلاد أخرى ، أصبح فحص الجنين أثناء الحمل - ممكنا ، للتأكد من وجود هذه الأمراض أو عدم وجودها ...

اذا كنت قد علمت أن فحص طفلك لكريات الدم المنجلية ايجابيا ، عندئذ ، من الضرورى لك أن تعرف ما اذا كان ذلك يعنى أن طفلك مصابا بالمرض المنجلى أو حاملا له ...

الدكتورة / سناء عادل سقف الحيط

بحث " فقر الدم المنجلى فى الكويت "

بالاتفاق مع : معهد الكويت للاختصاصات الطبيه

سناء عادل سقف الحيط
يوليو ١٩٩٠ - الكويت

Sana' Adel Saqf El-Hait
July 1990 - Kuwait

Appendix 4

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Abbreviations

SCD	Sickle cell disease
Hb	Haemoglobin
HB S	Sickle Haemoglobin
AS	Sickle cell trait carrier, heterozygous
SS	Sickle cell homozygous
β_2^S	Sickle beta chain
β thal	beta thalassaemia